

GenCore version 5.1.6  
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## OM protein - protein search, using sw model

Run on: July 2, 2003, 15:20:59 ; Search time 68 Seconds

(Without alignments)  
4606,944 Million cell updates/sec

Title: NP\_000123

Perfect score: 12418  
1 mgjelsstcflclrltfcfsa.....wvhlqalmevjgceagly 2351Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 908470 seqs, 133250620 residues

Total number of hits satisfying chosen parameters: 908470

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 08  
Maximum Match 1008  
Listing first 200 summaries

## Database :

A.Geneseq\_101002.\*  
1: /SID52/gcgdata/geneseq/geneseq-emb1/AA1980.DAT.\*  
2: /SID52/gcgdata/geneseq/geneseq-emb1/AA1981.DAT.\*  
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22: /SID52/gcgdata/geneseq/geneseq-emb1/AA2001.DAT.\*  
23: /SID52/gcgdata/geneseq/geneseq-emb1/AA2002.DAT.\*

Pred. No. is the number of results predicted by chance to have a  
score greater than or equal to the score of the result being printed,  
and is derived by analysis of the total score distribution.

## SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	12418	100.0	2351	6	AAp50059
2	12418	100.0	2351	18	AAW11329
3	12418	100.0	2351	19	AAW46245
4	12418	100.0	2351	19	AAW44373
5	12418	100.0	2351	21	AAV52537
6	12414	100.0	2351	18	AAW11435
7	12414	100.0	2351	18	AAW11416
8	12414	100.0	2351	18	AAW11343
9	12413	100.0	2351	18	AAW11461
10	12413	100.0	2351	18	AAW11445

11	12413	100.0	2351	18	AAW11425	Active Factor VIII
12	12413	100.0	2351	18	AAW11419	Active Factor VIII
13	12413	100.0	2351	18	AAW11398	Active Factor VIII
14	12413	100.0	2351	18	AAW11387	Active Factor VIII
15	12413	100.0	2351	18	AAW11362	Active Factor VIII
16	12412	100.0	2351	18	AAW81113	Factor VIII encode
17	12412	100.0	2351	18	AAW80959	Sequence of human
18	12412	100.0	2351	18	AAW11437	Active Factor VIII
19	12412	100.0	2351	18	AAW11427	Active Factor VIII
20	12412	100.0	2351	18	AAW11408	Active Factor VIII
21	12412	100.0	2351	18	AAW11347	Active Factor VIII
22	12412	100.0	2351	18	AAW11332	Active Factor VIII
23	12411	99.9	2351	18	AAW11396	Active Factor VIII
24	12411	99.9	2351	17	AAW00465	Factor-VIII. Homo
25	12409	99.9	2351	18	AAW11454	Active Factor VIII
26	12409	99.9	2351	22	AAW48843	Human factor VIII,
27	12409	99.9	2351	18	AAW11399	Active Factor VIII
28	12408	99.9	2351	18	AAW11404	Active Factor VIII
29	12408	99.9	2352	18	AAW11456	Active Factor VIII
30	12407.5	99.9	2352	18	AAW11458	Active Factor VIII
31	12407.5	99.9	2352	18	AAW11459	Active Factor VIII
32	12407.5	99.9	2352	18	AAW11463	Active Factor VIII
33	12407.5	99.9	2352	18	AAW11464	Active Factor VIII
34	12407.5	99.9	2352	18	AAW11438	Active Factor VIII
35	12407.5	99.9	2352	18	AAW11439	Active Factor VIII
36	12407.5	99.9	2352	18	AAW11442	Active Factor VIII
37	12407.5	99.9	2352	18	AAW11447	Active Factor VIII
38	12407.5	99.9	2352	18	AAW11450	Active Factor VIII
39	12407.5	99.9	2352	18	AAW11451	Active Factor VIII
40	12407.5	99.9	2352	18	AAW11423	Active Factor VIII
41	12407.5	99.9	2352	18	AAW11426	Active Factor VIII
42	12407.5	99.9	2352	18	AAW11429	Active Factor VIII
43	12407.5	99.9	2352	18	AAW11433	Active Factor VIII
44	12407.5	99.9	2352	18	AAW11406	Active Factor VIII
45	12407.5	99.9	2352	18	AAW11407	Active Factor VIII
46	12407.5	99.9	2352	18	AAW11412	Active Factor VIII
47	12407.5	99.9	2352	18	AAW11417	Active Factor VIII
48	12407.5	99.9	2352	18	AAW11418	Active Factor VIII
49	12407.5	99.9	2352	18	AAW11389	Active Factor VIII
50	12407.5	99.9	2352	18	AAW11394	Active Factor VIII
51	12407.5	99.9	2352	18	AAW11397	Active Factor VIII
52	12407.5	99.9	2352	18	AAW11400	Active Factor VIII
53	12407.5	99.9	2352	18	AAW11374	Active Factor VIII
54	12407.5	99.9	2352	18	AAW11381	Active Factor VIII
55	12407.5	99.9	2352	18	AAW11382	Active Factor VIII
56	12407.5	99.9	2352	18	AAW11385	Active Factor VIII
57	12407.5	99.9	2352	18	AAW11388	Active Factor VIII
58	12407.5	99.9	2352	18	AAW11357	Active Factor VIII
59	12407.5	99.9	2352	18	AAW11363	Active Factor VIII
60	12407.5	99.9	2352	18	AAW11364	Active Factor VIII
61	12407.5	99.9	2352	18	AAW11368	Active Factor VIII
62	12407.5	99.9	2352	18	AAW11372	Active Factor VIII
63	12407.5	99.9	2352	18	AAW11342	Active Factor VIII
64	12407.5	99.9	2352	18	AAW11344	Active Factor VIII
65	12407.5	99.9	2352	18	AAW11345	Active Factor VIII
66	12407.5	99.9	2352	18	AAW11350	Active Factor VIII
67	12407.5	99.9	2352	18	AAW11353	Active Factor VIII
68	12407.5	99.9	2352	18	AAW11354	Active Factor VIII
69	12407.5	99.9	2352	18	AAW11330	Active Factor VIII
70	12407.5	99.9	2352	18	AAW11333	Active Factor VIII
71	12407.5	99.9	2352	18	AAW11334	Active Factor VIII
72	12407.5	99.9	2352	18	AAW11336	Active Factor VIII
73	12407.5	99.9	2352	18	AAW11337	Active Factor VIII
74	12407.5	99.9	2352	18	AAW11352	Active Factor VIII
75	12406	99.9	2351	18	AAW11462	Active Factor VIII
76	12406	99.9	2351	18	AAW11376	Active Factor VIII
77	12403.5	99.9	2350	18	AAW11358	Active Factor VIII
78	12403.5	99.9	2350	18	AAW11359	Active Factor VIII
79	12403.5	99.9	2351	18	AAW10591	Factor VIII:C (Arg
80	12402	99.9	2351	18	AAW13496	Factor VIII:C (Arg
81	12402	99.9	2351	18	AAW13496	Factor VIII:C (Arg
82	12402	99.9	2351	18	AAW13496	Factor VIII:C (Arg
83	12402	99.9	2351	20	AAW21676	Factor VIII protei

84	12400	99.9	2351	18	AAWI10592	Factor VIII:C (FvF	157	12356	99.5	2343	18	AAWI1393	Active Factor VIII
85	12400	99.9	2351	18	AAWI1471	Active Factor VIII	158	12355	99.5	2342	18	AAWI1422	Active Factor VIII
86	12399.5	99.9	2350	18	AAWI1413	Active Factor VIII	159	12351.5	99.5	2344	18	AAWI1410	Active Factor VIII
87	12399.5	99.8	2351	18	AAWI1443	Active Factor VIII	160	12344.5	99.4	2342	18	AAWI11349	Active Factor VIII
88	12399	99.8	2351	18	AAWI1472	Active Factor VIII	161	12339	99.4	2351	7	AAW67941	Sequence of human
89	12398	99.8	2349	18	AAWI1424	Active Factor VIII	162	12311	99.2	2332	22	AAW11902	N-terminal truncat
90	12398	99.8	2351	18	AAWI1173	Active Factor VIII	163	12311	99.1	2332	18	AAW33223	Procogulant-activ
91	12398	99.8	2351	18	AAWI10590	Factor VIII:C (Phe	164	12306	99.1	2332	18	AAW33222	Procogulant-activ
92	12397.5	99.8	2350	18	AAWI1405	Active Factor VIII	165	12306	99.1	2332	18	AAW33225	Procogulant-activ
93	12397.5	99.8	2350	18	AAWI11346	Active Factor VIII	166	12303	99.1	2332	14	AAW33224	Procogulant-activ
94	12396.5	99.8	2350	18	AAWI1470	Active Factor VIII	167	12301	99.1	2332	18	AAW33227	Human Factor VIII
95	12396.5	99.8	2350	18	AAWI1375	Active Factor VIII	168	12301	99.1	2332	19	AAW33433	Human factor VIII
96	12396	99.8	2351	16	AAW87223	Human Factor-VIII	169	12301	99.1	2332	20	AAW11594	Human factor VIII
97	12395	99.8	2349	18	AAWI1460	Active Factor VIII	170	12301	99.1	2332	22	AAE10826	Human mature wild-
98	12395	99.8	2351	15	AAW5352	Sequence of human	171	12301	99.1	2332	22	AAE10826	Human factor VIII
99	12394.5	99.8	2350	18	AAWI1457	Active Factor VIII	172	12301	99.1	2332	22	AAW50465	Human factor VIII
100	12394.5	99.8	2350	18	AAWI1380	Active Factor VIII	173	12301	99.1	2332	23	AAU79869	Human factor VIII
101	12393.5	99.8	2348	18	AAWI1426	Active Factor VIII	174	12297	99.0	2332	23	AAU79870	Human factor VIII
102	12393	99.8	2349	18	AAWI1465	Active Factor VIII	175	12297	99.0	2332	23	AAU79872	Human factor VIII
103	12393	99.8	2349	18	AAWI1430	Active Factor VIII	176	12295	99.0	2332	18	AAW33226	Procogulant-activ
104	12393	99.8	2349	18	AAWI1366	Active Factor VIII	177	12295	99.0	2332	23	AAU79871	Human factor VIII
105	12392.5	99.8	2348	18	AAWI1395	Active Factor VIII	178	12293	99.0	2332	23	AAU79874	Human factor VIII
106	12392	99.8	2349	18	AAWI1420	Active Factor VIII	179	12291	99.0	2332	23	AAU79873	Human factor VIII
107	12392	99.8	2349	18	AAWI1448	Active Factor VIII	180	12283	98.9	2332	23	AAU79875	Human factor VIII
108	12392	99.8	2349	18	AAWI1338	Active Factor VIII	181	12261	98.7	2332	8	AAW71727	Factor VIII:C varia
109	12392	99.8	2351	8	AAW70448	Human factor VIII	182	12260	98.7	2332	8	AAW71729	Factor VIII:C varia
110	12391.5	99.8	2348	18	AAWI1444	Active Factor VIII	183	12258	98.7	2332	8	AAW71726	Factor VIII:C varia
111	12391.5	99.8	2348	18	AAWI1386	Active Factor VIII	184	12258	98.7	2332	21	AAW57847	Factor VIII:C varia
112	12391.5	99.8	2350	18	AAWI1339	Active Factor VIII	185	12251	98.7	2332	19	AAW44132	Human Factor VIII
113	12390.5	99.8	2348	18	AAWI1455	Active Factor VIII	186	12181	98.1	2332	21	AAW44132	Human Factor VIII
114	12390.5	99.8	2348	18	AAWI1378	Active Factor VIII	187	11955	96.1	2351	6	AAW50319	Human Factor VIII
115	12387	99.8	2347	18	AAWI1469		188	11955	96.1	2351	6	AAW50319	Human Factor VIII
116	12387	99.8	2347	18	AAWI1402	Active Factor VIII	189	9493	76.4	2343	21	AAW57846	Canine Factor VIII
117	12387	99.8	2347	18	AAWI1369	Active Factor VIII	190	9493	76.3	2343	20	AAW80989	Canine Factor VIII
118	12387	99.8	2349	18	AAWI1440	Active Factor VIII	191	8835	71.1	2319	19	AAW53485	Murine factor VIII
119	12387	99.8	2349	18	AAWI1401	Active Factor VIII	192	8835	71.1	2319	19	AAW44135	Mus musculus factor
120	12386.5	99.7	2348	18	AAWI1449	Active Factor VIII	193	8835	71.1	2319	20	AAW13156	Mouse factor VIII
121	12386.5	99.7	2349	18	AAWI1350	Active Factor VIII	194	8835	71.1	2319	22	AAW30467	Mouse factor VIII
122	12386	99.7	2349	18	AAWI1386	Active Factor VIII	195	8835	71.1	2319	22	AAW30467	Mouse factor VIII
123	12386	99.7	2349	18	AAWI1355	Active Factor VIII	196	8828	70.3	2304	21	AAW51202	Murine factor VIII
124	12385.5	99.7	2348	18	AAWI1414	Active Factor VIII	197	8730	67.3	2304	21	AAW57848	Mouse Factor VIII
125	12385	99.7	2347	18	AAWI11379	Active Factor VIII	198	8357	67.3	1661	18	AAW18640	Factor VIII-dB695
126	12382.5	99.7	2346	18	AAWI1434	Active Factor VIII	199	8076	65.0	2133	20	AAW31597	Porcine factor VIII
127	12382.5	99.7	2348	18	AAWI1448	Active Factor VIII	199	8076	65.0	2133	22	AAW50468	Porcine factor VIII
128	12382	99.7	2347	18	AAWI1467	Active Factor VIII	200	8070	65.0	2133	19	AAW44133	Sus scrofa factor
129	12379.5	99.7	2346	18	AAWI1452	Active Factor VIII							
130	12379	99.7	2347	18	AAWI1345	Active Factor VIII							
131	12378.5	99.7	2346	18	AAWI1462	Active Factor VIII							
132	12378.5	99.7	2348	18	AAWI1462	Active Factor VIII							
133	12378	99.7	2346	18	AAWI1341	Active Factor VIII							
134	12377.5	99.7	2345	18	AAWI1466	Active Factor VIII							
135	12376.5	99.7	2346	18	AAWI1421	Active Factor VIII							
136	12376.5	99.7	2346	18	AAWI1360	Active Factor VIII							
137	12376	99.7	2347	18	AAWI1351	Active Factor VIII							
138	12376	99.7	2347	18	AAWI1411	Active Factor VIII							
139	12375.5	99.7	2346	18	AAWI1421	Active Factor VIII							
140	12375.5	99.7	2346	18	AAWI1391	Active Factor VIII							
141	12374.5	99.6	2348	18	AAWI1367	Active Factor VIII							
142	12374.5	99.6	2346	18	AAWI1392	Active Factor VIII							
143	12374	99.6	2345	18	AAWI1394	Active Factor VIII							
144	12372.5	99.6	2345	18	AAWI1446	Active Factor VIII							
145	12372	99.6	2345	18	AAWI1356	Active Factor VIII							
146	12371.5	99.6	2344	18	AAWI1453	Active Factor VIII							
147	12371	99.6	2345	18	AAWI1432	Active Factor VIII							
148	12370.5	99.6	2344	18	AAWI1383	Active Factor VIII							
149	12368	99.6	2345	18	AAWI1331	Active Factor VIII							
150	12366.5	99.6	2344	18	AAWI1348	Active Factor VIII							
151	12366.5	99.6	2344	18	AAWI1361	Active Factor VIII							
152	12366	99.6	2344	18	AAWI1370	Active Factor VIII							
153	12366	99.6	2345	18	AAWI1441	Active Factor VIII							
154	12365	99.6	2345	18	AAWI1415	Active Factor VIII							
155	12362	99.5	2345	18	AAWI1403	Active Factor VIII							
156	12358.5	99.5	2343	18	AAWI1335	Active Factor VIII							
					AAWI1384	Active Factor VIII							
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PI Capon DJ, Vohar GA, Lawn RM, Wood WI;  
XX WPI: 1985-277976/45.  
DR N-PSDB: AAN50054.  
XX  
PT New recombinant functional human factor VIII or deriv. - useful for  
PT treating haemophilia and obtd. as pure prod. by recombinant DNA  
PT technology.  
XX  
XX Disclosure: Fig. 10a(10-10C(III)); 109pp; English.  
XX  
XX The sequence is that of human factor VIII. Amino acids 1-19 are the  
XX predicted signal peptide, and amino acids 1-2337 are the predicted  
XX mature protein. The protein is produced in pure form and in useful  
XX amounts, using recombinant DNA techniques. Factor VIII can be used  
XX to correct factor VIII deficient plasma, and activates factor X to  
XX Xa in the presence of factor IXa, Ca and phospholipid. These to  
XX activites are inactivated by antibodies specific for factor VIII.  
XX The activity of the prod. is bound to an immobilised monoclonal  
XX antibody specific for factor VIII. Factor VIII activity is  
XX activated by thrombin. The activity is bound to, and can be eluted  
XX from, immobilised von Willebrand factor. Dose of factor VIII is  
XX 20-40 units/kg over 8 hours i.v. for maintenance therapy for  
XX haemophilia. 40 units/kg for preoperative conditions, or 15-20  
XX units/kg for minor haemorrhaging.  
SQ Sequence 2351 AA:  
Query Match 100.0%; Score 12418; DB 6; Length 2351;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 0; Gaps 0;  
QY 1 MQEISTCFELLCIFRCFSATRRYYLGAVELSDMYQSDGLGELPYDAFPPRPKSPNN 60  
DB 1 MQEISTCFELLCIFRCFSATRRYYLGAVELSDMYQSDGLGELPYDAFPPRPKSPNN 60  
QY 61 TSVYKKTLFVEPTDHLFNIAKPRPPMGLGTTIAEYDVTYTLTKNASHVSLHAY 120  
DB 61 TSVYKKTLFVEPTDHLFNIAKPRPPMGLGTTIAEYDVTYTLTKNASHVSLHAY 120  
QY 121 GSVYKASBGAEDYDQTSOREKEDKYFPGSHTYVVOYLKENGPMASDPLCLTYSTLSH 180  
DB 121 GSVYKASBGAEDYDQTSOREKEDKYFPGSHTYVVOYLKENGPMASDPLCLTYSTLSH 180  
QY 121 GSVYKASBGAEDYDQTSOREKEDKYFPGSHTYVVOYLKENGPMASDPLCLTYSTLSH 180  
DB 121 GSVYKASBGAEDYDQTSOREKEDKYFPGSHTYVVOYLKENGPMASDPLCLTYSTLSH 180  
QY 181 VDLKDLNSGLIGALLVREGSLAKETQTLNKFILLFAVPEGKSMHSETKNSLMODRD 240  
DB 181 VDLKDLNSGLIGALLVREGSLAKETQTLNKFILLFAVPEGKSMHSETKNSLMODRD 240  
QY 181 VDLKDLNSGLIGALLVREGSLAKETQTLNKFILLFAVPEGKSMHSETKNSLMODRD 240  
DB 181 VDLKDLNSGLIGALLVREGSLAKETQTLNKFILLFAVPEGKSMHSETKNSLMODRD 240  
QY 241 AASARAPKMHYVNGVYVNSRLPGLIGCHRRKSVYMHVIGMTPPEVHSTIEGHTFLVRNH 300  
DB 241 AASARAPKMHYVNGVYVNSRLPGLIGCHRRKSVYMHVIGMTPPEVHSTIEGHTFLVRNH 300  
QY 301 ROGLSEISPTFLTAQTLLMDGOELLFCHISSHQDGMKAEVYKVDSCPEEPOLRMKNNE 360  
DB 301 ROGLSEISPTFLTAQTLLMDGOELLFCHISSHQDGMKAEVYKVDSCPEEPOLRMKNNE 360  
QY 301 ROGLSEISPTFLTAQTLLMDGOELLFCHISSHQDGMKAEVYKVDSCPEEPOLRMKNNE 360  
DB 301 ROGLSEISPTFLTAQTLLMDGOELLFCHISSHQDGMKAEVYKVDSCPEEPOLRMKNNE 360  
QY 361 EAEYDQDGLDSEMDYVRRPDDNSPFTQIRSAKKNHKTWNYHIAAEEDMYAPLYLA 420  
DB 361 EAEYDQDGLDSEMDYVRRPDDNSPFTQIRSAKKNHKTWNYHIAAEEDMYAPLYLA 420  
QY 421 PDDRSYKSOYLNNGPORGIRKKYKVRPMAYTDEFKTRBAIOHESGILGPLLYGEVNDL 480  
DB 421 PDDRSYKSOYLNNGPORGIRKKYKVRPMAYTDEFKTRBAIOHESGILGPLLYGEVNDL 480  
QY 481 LIIFKNASRPYNIYHGHITDVRPLYSRLPKVCKHLKDFPLPEIFIKYKWTYVDCP 540  
DB 481 LIIFKNASRPYNIYHGHITDVRPLYSRLPKVCKHLKDFPLPEIFIKYKWTYVDCP 540  
QY 541 TKSDPCLTRYSSFFYNMERDLASGLIGPLLICYSVDORONQMSKRNVLFSVDE 600  
DB 541 TKSDPCLTRYSSFFYNMERDLASGLIGPLLICYSVDORONQMSKRNVLFSVDE 600  
QY 601 NRSWYLTENIQRFPLPAGVQLEDPERQASINMHSINGYVPSLQSLVCLHEVAYWTLS 660

DB 601 NRSWYLTENIQRFPLPAGVQLEDPERQASINMHSINGYVPSLQSLVCLHEVAYWTLS 660  
QY 661 IGAQDPLSVFSGYTFKKKMYEDDTLTLPFGGEVFWMSKENPGLMTLGGHNSDRNRG 720  
DB 661 IGAQDPLSVFSGYTFKKKMYEDDTLTLPFGGEVFWMSKENPGLMTLGGHNSDRNRG 720  
QY 721 MTALLKYSQDKKTYGDIYEDYEDISAVILSKNNALIEPFSQNSRHRSTQOFNATTT 780  
DB 721 MTALLKYSQDKKTYGDIYEDYEDISAVILSKNNALIEPFSQNSRHRSTQOFNATTT 780  
QY 781 PENDIEKTFWFHARTPMPKIQONVSSDLMTLRQSPFHGSLSDLOEAKETFSDDPS 840  
DB 781 PENDIEKTFWFHARTPMPKIQONVSSDLMTLRQSPFHGSLSDLOEAKETFSDDPS 840  
QY 841 PGALDSNNLSSEMTHTRRQLHSGDMYFTEPSGLOLRNEXIGTTAAETELKIDPKVSS 900  
DB 841 PGALDSNNLSSEMTHTRRQLHSGDMYFTEPSGLOLRNEXIGTTAAETELKIDPKVSS 900  
QY 901 SNNLISTIPSDNLAAGTDNTSLGPPSPVHYDSQDITLFGKSSPLTESGPLSLEE 960  
DB 901 SNNLISTIPSDNLAAGTDNTSLGPPSPVHYDSQDITLFGKSSPLTESGPLSLEE 960  
QY 961 NNDKLESGILMNSOESSMGKVVSTESGRJFGKRAHGPALLTRDNALFRVYSILKTN 1020  
DB 961 NNDKLESGILMNSOESSMGKVVSTESGRJFGKRAHGPALLTRDNALFRVYSILKTN 1020  
QY 1021 KTSNNSATNRKTHIDGSLLENSPVMONILSDTEFKKVTPLIHDMLMDKATLRL 1080  
DB 1021 KTSNNSATNRKTHIDGSLLENSPVMONILSDTEFKKVTPLIHDMLMDKATLRL 1080  
QY 1081 NMSNKTSTSKNNEMVQOKKEGPIPPDAQNPDMSFFKMLFELPSARWIOPTHGKNSLNG 1140  
DB 1081 NMSNKTSTSKNNEMVQOKKEGPIPPDAQNPDMSFFKMLFELPSARWIOPTHGKNSLNG 1140  
QY 1141 QGSPKQVLSGPEKVEGONFLSKNNVYVGGEPFKVGLKEMVPSNNLTLTMDN 1200  
DB 1141 QGSPKQVLSGPEKVEGONFLSKNNVYVGGEPFKVGLKEMVPSNNLTLTMDN 1200  
QY 1201 LHENNTNOKKIQEIEKEKTELQENNVLPQIHVYTGKKNPKMLFLSTRONVBSYD 1260  
DB 1201 LHENNTNOKKIQEIEKEKTELQENNVLPQIHVYTGKKNPKMLFLSTRONVBSYD 1260  
QY 1261 GAYAPVLQDPRSLNDSTNRKTHAHFSKKEEENLEGNGTKQIVKACTTRISPNT 1320  
DB 1261 GAYAPVLQDPRSLNDSTNRKTHAHFSKKEEENLEGNGTKQIVKACTTRISPNT 1320  
QY 1321 SQONFVYORSKRALKQFLPLETELEKRIIVDTSTQNSKNNKHLTSTLTQIDYNEKE 1380  
DB 1321 SQONFVYORSKRALKQFLPLETELEKRIIVDTSTQNSKNNKHLTSTLTQIDYNEKE 1380  
QY 1381 KGATIOSPLSDCLTRSHSIPQANRSPRLIAVSSFPISIRIYLTFLQDNSSHLPAASY 1440  
DB 1381 KGATIOSPLSDCLTRSHSIPQANRSPRLIAVSSFPISIRIYLTFLQDNSSHLPAASY 1440  
QY 1441 RKDSGVQESHSFLQAKKNNLSLILLEMTGQORVSGISGTSATNVTYKKVENYVLP 1500  
DB 1441 RKDSGVQESHSFLQAKKNNLSLILLEMTGQORVSGISGTSATNVTYKKVENYVLP 1500  
QY 1501 KPDLPKTSQKVELLPVNIYQKDFPTETSNGSPGHLDESSLDGTGCAIKWNEANRP 1560  
DB 1501 KPDLPKTSQKVELLPVNIYQKDFPTETSNGSPGHLDESSLDGTGCAIKWNEANRP 1560  
QY 1561 GKVPFLRATRESSAKTPSKLDPLAMDHNHYGTQIPKEEMKSOEKSPKTAFAKKDITLSL 1620  
DB 1561 GKVPFLRATRESSAKTPSKLDPLAMDHNHYGTQIPKEEMKSOEKSPKTAFAKKDITLSL 1620  
QY 1621 NACESNHAIAINEGONKEIEIVTAKGGRERLCSQNPVYLAKHOREITRTTLOSQOE 1680  
DB 1621 NACESNHAIAINEGONKEIEIVTAKGGRERLCSQNPVYLAKHOREITRTTLOSQOE 1680  
QY 1681 IDYDITISVEKKEDPDIDYEDENQSPRSFOKTRHFIAAVERLMDYGMSSPHVLNR 1740  
DB 1681 IDYDITISVEKKEDPDIDYEDENQSPRSFOKTRHFIAAVERLMDYGMSSPHVLNR 1740

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Db      1681 IDYDTISVEKKKEDFDIYDENQSPRSFOKTRHYFAAVERLMDYGSPPHLNR 1740
Qy      1741 AOSGSVPQFKKVVQOETDSSFTQPIYRGELNEHGLIGPTIRAEVDNMTYFRNQS 1800
Db      1741 AOSGSVPQFKKVVQOETDSSFTQPIYRGELNEHGLIGPTIRAEVDNMTYFRNQS 1800
Qy      1801 PYSFYSLSIYEEDQOGAEPRKRVKPNKTYTFWKVQHHMAFTKDEPDCAMAFESDV 1860
Db      1801 PYSFYSLSIYEEDQOGAEPRKRVKPNKTYTFWKVQHHMAFTKDEPDCAMAFESDV 1860
Qy      1861 DEKDVHSGILGIPLVCHTNTLPNPAHROYVQOEFALFEFTTFDETKSYTEMENRCA 1920
Db      1861 DEKDVHSGILGIPLVCHTNTLPNPAHROYVQOEFALFEFTTFDETKSYTEMENRCA 1920
Qy      1921 PCNIOMEDPTEKENVRRHAINGYIMDTLPGLVMAODORIRWYLLSMGSNENHSHFSGH 1980
Db      1921 PCNIOMEDPTEKENVRRHAINGYIMDTLPGLVMAODORIRWYLLSMGSNENHSHFSGH 1980
Qy      1981 VFTVRRKEEYKMALYNLYPGVFETVEMLPKAGIRVRECLIGEHLHAGMSTLFLVYSNKC 2040
Db      1981 VFTVRRKEEYKMALYNLYPGVFETVEMLPKAGIRVRECLIGEHLHAGMSTLFLVYSNKC 2040
Qy      2041 QTPPLGASGHTRDQITASQCYQMAPKLARLHYSGSINAMSTEKEPSWIKVDLLAPMII 2100
Db      2041 QTPPLGASGHTRDQITASQCYQMAPKLARLHYSGSINAMSTEKEPSWIKVDLLAPMII 2100
Qy      2101 HGKTQGAROKFSSLYISQFTIMYSIDGKKMOTYRGNSTGTLMVFQGVNDSSGIRKHNIPN 2160
Db      2101 HGKTQGAROKFSSLYISQFTIMYSIDGKKMOTYRGNSTGTLMVFQGVNDSSGIRKHNIPN 2160
Qy      2161 PPTIARYTRLPHTYSTRSTLRMEIMGCDLNSCMPILMESKATSDQITASSYFTNMRA 2220
Db      2161 PPTIARYTRLPHTYSTRSTLRMEIMGCDLNSCMPILMESKATSDQITASSYFTNMRA 2220
Qy      2221 TWSPSKARLHLQGRSNMARPQVNNKEMLVDFQTKMVTGYTTQGVKSLTSMYKEFL 2280
Db      2221 TWSPSKARLHLQGRSNMARPQVNNKEMLVDFQTKMVTGYTTQGVKSLTSMYKEFL 2280
Qy      2281 ISSQDGHQWTLFPQNGKVVYFQGNQDSFPPVNSLDPPLLTRRLRHPQSWHQTALNM 2340
Db      2281 ISSQDGHQWTLFPQNGKVVYFQGNQDSFPPVNSLDPPLLTRRLRHPQSWHQTALNM 2340
Qy      2341 EYLGEADPLY 2351
Db      2341 EYLGEADPLY 2351

RESULT 2
AAM11329
ID      AAM11329 standard; Protein: 2351 AA.
XX
AC      AAM11329;
XX
DT      17-NOV-1997 (first entry)
XX
DE      Native Factor VIII:C.
XX
KW      Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW      fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW      plasma protease; thrombin; immunogen; antibody; haemophilia; therapy;
KW      proteolytic cleavage.
XX
OS      Homo sapiens.
XX
FH      Key
FT      Peptide
FT      Location/Qualifiers
FT      /note= "signal peptide"
FT      Protein
FT      /note= "mature Factor VIII:C"
FT      Region
FT      /note= "heavy chain fragment"
FT      1668..2350
FT      Region
FT      /note= "light chain fragment"

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FT      Domain 760..1667
FT      /note= "B domain"
XX
XX      MO9703195-A1.
XX
XX      30-JAN-1997.
XX
XX      09-JUL-1996; 96MO-US11444.
XX
XX      11-JUL-1995; 95DS-0001025.
XX
XX      (CHIR ) CHIRON CORP.
XX
XX      Cohen FE, Hung DT, Innis M;
XX
XX      WPI: 1997-119050/11.
XX      N-PSDB: AAT51357.
XX
XX      Factor VIII:C analog modified adjacent to a non-activating Arg
XX      residue - used in the treatment of haemophiliacs, by improvement of
XX      haemostasis
XX
XX      Disclosure: Fig 1; 90pp; English.
XX
XX      This sequence represents the native Factor VIII:C. Factor VIII:C is a
XX      large glycoprotein that participates in the blood coagulation cascade
XX      that ultimately converts soluble fibrinogen to insoluble fibrin clot,
XX      effecting haemostasis. A deficiency in Factor VIII:C is responsible for
XX      haemophilia A, which is an X-chromosome-linked inherited bleeding
XX      diathesis. Factor VIII:C is activated by plasma proteases, such as
XX      thrombin. During activation the mature polypeptide is cleaved to
XX      generate heavy and light chain fragments that are further cleaved. The
XX      DNA encoding this sequence is mutated, using mutagenic primers, to
XX      produce the active Factor VIII:C analogues of the invention (such as
XX      AAM11330). The analogues comprise a native Factor VIII:C polypeptide
XX      modified at a site adjacent to a non-activating Arg residue so that a
XX      Arg-Pro or Pro-Arg dipeptide is created. Complexes of two or more of the
XX      analogues, nucleic acids and vectors encoding them may be used alone or
XX      in conjunction with each other, for the prevention or treatment of active
XX      Factor VIII:C deficiency in a mammal. The analogues may be used as
XX      immunogens to raise antibodies, and in the treatment of haemophiliacs, by
XX      improvement of haemostasis. The analogues are resistant to proteolytic
XX      cleavage and display increased plasma half-life. They may be administered
XX      at lower dosages and by different modes of administration.
XX
XX      Sequence 2351 AA:
XX
XX      Query Match 100.0%; Score 12418; DB 18; Length 2351;
XX      Best local Similarity 100.0%; Pred. No. 0;
XX      Matches 2351; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
XX
Qy      1 MOELSTCFPLCLLRCSATRRYLGAVELSMYQMSDGLPVDARPPRPVPSPPN 60
Db      1 MOELSTCFPLCLLRCSATRRYLGAVELSMYQMSDGLPVDARPPRPVPSPPN 60
Qy      61 TSVYKKTLFEFTDHLFNIAKRRPMMGLGPTIOAEVYDVVITLKNMASHVSLAH 120
Db      61 TSVYKKTLFEFTDHLFNIAKRRPMMGLGPTIOAEVYDVVITLKNMASHVSLAH 120
Qy      121 GVSYWKASBEAEVDQTSOREKEDDKVPPGSSHYVQVLYKENGPMASDPLCLTYSYLSH 180
Db      121 GVSYWKASBEAEVDQTSOREKEDDKVPPGSSHYVQVLYKENGPMASDPLCLTYSYLSH 180
Qy      181 VDLVNDNSGLIGALLVCREGSLAREKQTLHKFTLLFAVDEGKSMHSETNLSMDORD 240
Db      181 VDLVNDNSGLIGALLVCREGSLAREKQTLHKFTLLFAVDEGKSMHSETNLSMDORD 240
Qy      241 AASARAMPKMTVNGVYVNSRLPGLIGCRKSVYWHVGMGTPEVHSIFLEGHTFLVANH 300
Db      241 AASARAMPKMTVNGVYVNSRLPGLIGCRKSVYWHVGMGTPEVHSIFLEGHTFLVANH 300
Qy      301 ROASLEISPTFTLAQTLMDLGQFLFCCHISSHQDGMKAYKVKVDSCEPQLMKRNE 360
Db      301 ROASLEISPTFTLAQTLMDLGQFLFCCHISSHQDGMKAYKVKVDSCEPQLMKRNE 360

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301 RQASLEISPIITFLTAQTLLMDLGOFLFLFCHISHQHOGMEAYKVDSCPEPRLRKKNNE 360  
361 EAEYDDDLTDEEMOVYRFDDDNPSFIOIRSAKAKHKKTMVHYTIAEEEDMDYAPVIA 420  
361 EAEYDDDLTDEEMOVYRFDDDNPSFIOIRSAKAKHKKTMVHYTIAEEEDMDYAPVIA 420  
421 PDDRSYKSOYLANKGQIRGRKTKKVRMAYTDETKTNEAIOHESGILGFLYGEYDTL 480  
421 PDDRSYKSOYLANKGQIRGRKTKKVRMAYTDETKTNEAIOHESGILGFLYGEYDTL 480  
481 LIIFKNOASRPYNIYPHGITDVRPLYSRLPKGVNHLKDPFILGELFEKKYKMTVVEDP 540  
481 LIIFKNOASRPYNIYPHGITDVRPLYSRLPKGVNHLKDPFILGELFEKKYKMTVVEDP 540  
541 TKSDPRLCTFRYYSFVNNERDLASGLIGLPLLCYKESVDQGNQIMSDKRNVLFSVDE 600  
541 TKSDPRLCTFRYYSFVNNERDLASGLIGLPLLCYKESVDQGNQIMSDKRNVLFSVDE 600  
601 NRSWYLTENIORFLPNPAGVQLEDPEFOASNIHSHNGYVFDISQISVCLHEVAYYTLIS 660  
601 NRSWYLTENIORFLPNPAGVQLEDPEFOASNIHSHNGYVFDISQISVCLHEVAYYTLIS 660  
661 IGAOTDFLSYFSGTFRKHKMYEDTLTFPPSGEYFKSMENPGMLILCHNSDFRNG 720  
661 IGAOTDFLSYFSGTFRKHKMYEDTLTFPPSGEYFKSMENPGMLILCHNSDFRNG 720  
721 MTALLKVSCKNDYEDYEDYEDISAYLLSKNNAIEPRSFSONSRHPSTROKOFNATTI 780  
721 MTALLKVSCKNDYEDYEDYEDISAYLLSKNNAIEPRSFSONSRHPSTROKOFNATTI 780  
781 PENDIEKTDWFAHRTPMRKIQNVSSSDLLMLRQSPTPHGLSLSDLOEKYETFEEDPS 840  
781 PENDIEKTDWFAHRTPMRKIQNVSSSDLLMLRQSPTPHGLSLSDLOEKYETFEEDPS 840  
841 PGALDSNNSLSEKTHFRPOLHSGDMYFEPESGLQRLNEXLIGTATTELKIDFVSVST 900  
841 PGALDSNNSLSEKTHFRPOLHSGDMYFEPESGLQRLNEXLIGTATTELKIDFVSVST 900  
901 SNNLISTIPBDNLAGTONTSLGPRSPMRYHYSQIDTTLTGKKSPLTSSGGPLSLSE 960  
901 SNNLISTIPBDNLAGTONTSLGPRSPMRYHYSQIDTTLTGKKSPLTSSGGPLSLSE 960  
961 NNSDKLLESGLMNSOBSSMGKNVSTESGRLFEKGRAHGAPALLTKDNALFKVVISILKTN 1020  
961 NNSDKLLESGLMNSOBSSMGKNVSTESGRLFEKGRAHGAPALLTKDNALFKVVISILKTN 1020  
1021 KTSNNSATNRKTHIDGPSLLIENSPYMONILIESDTEEFKAYPLIHDRLMDKNATATRL 1080  
1021 KTSNNSATNRKTHIDGPSLLIENSPYMONILIESDTEEFKAYPLIHDRLMDKNATATRL 1080  
1081 NHRNKNKTTSSKNMENVQOKKEGPIPPDAONPDMSFPKMLFLPESARNIORTHGKNSLNG 1140  
1081 NHRNKNKTTSSKNMENVQOKKEGPIPPDAONPDMSFPKMLFLPESARNIORTHGKNSLNG 1140  
1141 QGSPKOLVSLGPEKSVBQNFLESEKKNVVGGEFTKDVGLKEVPEPSSNLEPLNLNDN 1200  
1141 QGSPKOLVSLGPEKSVBQNFLESEKKNVVGGEFTKDVGLKEVPEPSSNLEPLNLNDN 1200  
1201 LHENNTHNOEKKIOEIEIEKKEFTLQIENVVLPQIHTVGTGKNMKNLELLSTRONVGSYD 1260  
1201 LHENNTHNOEKKIOEIEIEKKEFTLQIENVVLPQIHTVGTGKNMKNLELLSTRONVGSYD 1260  
1261 GAYAPVLQDFRSLNDSTNRKTKHTAHFSKGEENLEGLGNOTQOIEVKACTTRISPNT 1320  
1261 GAYAPVLQDFRSLNDSTNRKTKHTAHFSKGEENLEGLGNOTQOIEVKACTTRISPNT 1320  
1321 SOONFVYQBSKRALQKQRLPLEETELERKRIIVYDSTQMSKMKHLTPSLTQIDYNEKE 1380  
1321 SOONFVYQBSKRALQKQRLPLEETELERKRIIVYDSTQMSKMKHLTPSLTQIDYNEKE 1380  
1381 KGATIOSPLSDCLTRSHSTIPQANSPLPIAKVSSFSFIRPYLTRYVLFQDNSSHLPAAST 1440  
1381 KGATIOSPLSDCLTRSHSTIPQANSPLPIAKVSSFSFIRPYLTRYVLFQDNSSHLPAAST 1440

1441 RKKDSGOESSHFLQGAKKKNNSLAILTLFEMTGQDREVSIGTSATNSVYTKKVENTVLP 1500  
1441 RKKDSGOESSHFLQGAKKKNNSLAILTLFEMTGQDREVSIGTSATNSVYTKKVENTVLP 1500  
1501 KPDLPRTSGKVELLPKHYIYOKDLPPTETSNQSGHDLVBSGLQGTGCAIKNENR 1560  
1501 KPDLPRTSGKVELLPKHYIYOKDLPPTETSNQSGHDLVBSGLQGTGCAIKNENR 1560  
1561 GRVPLRVATSSAKTPSKLLPRLANDNHVGTQIPEKEMKSOEKSEPTAKRKDTLLST 1620  
1561 GRVPLRVATSSAKTPSKLLPRLANDNHVGTQIPEKEMKSOEKSEPTAKRKDTLLST 1620  
1621 NACESNHAIAAINGQONKPEIEYTNAKQRTERLCSQNPVLAIRHORETTRTQSDQEE 1680  
1621 NACESNHAIAAINGQONKPEIEYTNAKQRTERLCSQNPVLAIRHORETTRTQSDQEE 1680  
1681 IDYDPTISVEKKEDFDIYDEDNQSPSPQKTRHYFIAAVERLMDYGMSSPHVLRNR 1740  
1681 IDYDPTISVEKKEDFDIYDEDNQSPSPQKTRHYFIAAVERLMDYGMSSPHVLRNR 1740  
1741 AOGSGVQPKVYVQOEFTDGFQPLVYGELENHGLGGLYTRAEDNIMYTRRNQSR 1800  
1741 AOGSGVQPKVYVQOEFTDGFQPLVYGELENHGLGGLYTRAEDNIMYTRRNQSR 1800  
1801 PYSFYSLSLSTEEDQROGAEPRKKNFYKNETKTYFMKVQHHMAPTKDEFDCKANAYFSDV 1860  
1801 PYSFYSLSLSTEEDQROGAEPRKKNFYKNETKTYFMKVQHHMAPTKDEFDCKANAYFSDV 1860  
1861 DLEKDVHSGLIGPLVCHNTLTPAHAGROYVQFALFPTIPDETKNWYETTENNERCRA 1920  
1861 DLEKDVHSGLIGPLVCHNTLTPAHAGROYVQFALFPTIPDETKNWYETTENNERCRA 1920  
1921 PCNIOWEDPTEKENVYRPHALNGYIMDTLPGLVMAQODRIMYLLSGNSMENHSHIFSGH 1980  
1921 PCNIOWEDPTEKENVYRPHALNGYIMDTLPGLVMAQODRIMYLLSGNSMENHSHIFSGH 1980  
1981 VFTVYKREKEXKMAIXNYXRGVETVYKMLPSKAGIMRRECLIGHILAGSFTLYVSNKC 2040  
1981 VFTVYKREKEXKMAIXNYXRGVETVYKMLPSKAGIMRRECLIGHILAGSFTLYVSNKC 2040  
2041 QTPPLGASGHTRDQITASGOYQMAPIRLARLHYSGISINMSTKEPFSIKYDLPAMIT 2100  
2041 QTPPLGASGHTRDQITASGOYQMAPIRLARLHYSGISINMSTKEPFSIKYDLPAMIT 2100  
2101 HGKKTQGAOKFSSLYISOPTIMYSLDGKKQTYRGNSTGTLLWFFPGVNDSSGIKHNIFN 2160  
2101 HGKKTQGAOKFSSLYISOPTIMYSLDGKKQTYRGNSTGTLLWFFPGVNDSSGIKHNIFN 2160  
2161 PPIIARYIRLPHPTYSIRSTLRMELGCDLNSCMPLGMSKASIDAOITASSYFTNNFA 2220  
2161 PPIIARYIRLPHPTYSIRSTLRMELGCDLNSCMPLGMSKASIDAOITASSYFTNNFA 2220  
2221 TWSPKARLHIOGRSNMROVNNPKEMLOYDFOKTKYVGTQGVKSLTSMYVEFL 2280  
2221 TWSPKARLHIOGRSNMROVNNPKEMLOYDFOKTKYVGTQGVKSLTSMYVEFL 2280  
2281 ISSSDQGHQWTLFPQNGKRVYVQGNDSFTPVNSLDPRLTTRYLRIRHOSVHQIALRM 2340  
2281 ISSSDQGHQWTLFPQNGKRVYVQGNDSFTPVNSLDPRLTTRYLRIRHOSVHQIALRM 2340  
2341 EYVAGEADQPLY 2351  
2341 EYVAGEADQPLY 2351

RESULT 3

ID AAM46245 standard; Protein: 2351 AA.

AC AAM46245;

DT 06-AUG-1998 (first entry)

XX Human factor III protein sequence.  
DE  
XX  
XX Replication defective: recombinant retrovirus; RRV; therapeutic protein;  
KW haemophilia; thrombosis; hypercoagulable disorder; liver disease; human;  
KW hepatitis; thalassemia; phenylketonuria; Lesch-Nyhan syndrome; diabetes;  
KW cystic fibrosis; Duchenne's Muscular Dystrophy; hypercholesterolemia;  
KW hypopituitarism; adenine deaminase deficiency; HIV infection; anaemia;  
KW Guacher's syndrome; high blood pressure; Alzheimer's disease; factor III;  
KW autoimmune; inflammatory disease.  
OS  
XX Homo sapiens.  
OS  
XX MO9800541-A2.  
XX  
XX 08-JAN-1998.  
XX  
XX 02-JUL-1997; 97MO-US11784.  
XX  
XX 04-JUN-1997; 97US-0869309.  
XX 03-JUL-1996; 96US-0645601.  
XX 13-AUG-1996; 96US-0696381.  
XX  
XX (CHIR ) CHIRON CORP.  
XX  
XX Allen JR, Barber JR, Boder M, Chang SMW, Chong K;  
PI De La Vega D, Depoloni J, Greengard J, Hsu DC, Ibanez CE;  
PI Jolly DJ, Lee R, Mittelstaedt DM, Prussak CE, Respass JG;  
XX  
XX WPI: 1998-086966/08.  
XX N-PSDB; AAV19380.  
XX  
XX New replication defective recombinant retro-viruses - which can be  
PT administered to provide long term systemic expression of therapeutic  
PT protein in blood, useful in, e.g. treating hyper-coagulable  
PT disorders  
XX  
XX  
XX Example 28; Pages 203-210; 272pp; English.  
XX  
XX This is the human factor III sequence. The encoding DNA is in the  
CC construction of recombinant retroviral vectors expressing human  
CC factor VIII. The specification provides the preparation of replication  
CC defective recombinant retrovirus (RRV) expressing a therapeutic protein.  
CC The RRV preparation is resistant to degradation by human complement and  
CC is capable of inducing long term systemic expression of the therapeutic  
CC protein when administered intravenously to a human. The long term  
CC systemic expression results in a measurable level of the therapeutic  
CC protein being produced in the blood of the human for a period of at least  
CC 30 days after the administration of the RRV vector preparation. RRV's can  
CC be used for in vivo delivery of therapeutic protein to treat, e.g.  
CC haemophilia A, haemophilia B, thrombosis, hypercoagulable disorders,  
CC liver diseases such as hepatitis, disorders such as thalassemia,  
CC phenylketonuria, Lesch-Nyhan syndrome, severe combined immunodeficiency  
CC (SCID), cystic fibrosis, Duchenne's Muscular Dystrophy, inherited  
CC emphysema, familial hypercholesterolemia, diabetes, hypopituitarism,  
CC adenine deaminase deficiency, alpha1-antitrypsin deficiency, Guacher's  
CC syndrome, anaemia, infections such as HIV infection, high blood pressure,  
CC Alzheimer's disease, autoimmune or inflammatory disease or graft versus  
CC host disease. RRV's are capable of surviving inactivation in human serum  
CC thereby allowing efficient gene transfer over prolonged periods of time.  
XX  
XX Sequence 2351 AA:  
SQ  
Query Match 100.0%; Score 12418; DB 19; Length 2351;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Db  
61 TSVYKKTLFVEFTDHLFNIAKRPMMGLGPTTQAEEYDVTITLKNMASHPVSLAAV 120  
121 GSYKASGEAEYDDTSQREKEDKVPFGSGSHYVQVULKENGPMASDPLCLYSLSH 180  
121 GSYKASGEAEYDDTSQREKEDKVPFGSGSHYVQVULKENGPMASDPLCLYSLSH 180  
181 VDLVDLNSGLIGALLVCREGSLAEKQTLAKETILLFAVDEGKSMHSETKNSLMODRD 240  
181 VDLVDLNSGLIGALLVCREGSLAEKQTLAKETILLFAVDEGKSMHSETKNSLMODRD 240  
241 AASARAMPKMTVNGVYNSRLPGILGCRKSVYVHVIQMGTPPEVHSIFLEGHTFLVRNH 300  
241 AASARAMPKMTVNGVYNSRLPGILGCRKSVYVHVIQMGTPPEVHSIFLEGHTFLVRNH 300  
301 ROASLEISPIFELTAQRLTMDAGQFLRCHLSSHQHGMAVYKXVDSCEPPOLRMKNNE 360  
301 ROASLEISPIFELTAQRLTMDAGQFLRCHLSSHQHGMAVYKXVDSCEPPOLRMKNNE 360  
361 EADYDDDLTSEMDVVRPDDNSPFIQIRSVAKKHPTKWHTYIAEBEDMDYAPLVLA 420  
361 EADYDDDLTSEMDVVRPDDNSPFIQIRSVAKKHPTKWHTYIAAEEDMDYAPLVLA 420  
421 PDDRSYKQYLNNGPQRIGRKYKRYFMAVYDEFTKTRALQHESGILGPLLYGEVDTL 480  
421 PDDRSYKQYLNNGPQRIGRKYKRYFMAVYDEFTKTRALQHESGILGPLLYGEVDTL 480  
481 LIIFKNOASRPYNYIPHGINDVAPLYSRRLPKGYKHLKDPILPGEIFKYMTVTEGDP 540  
481 LIIFKNOASRPYNYIPHGINDVAPLYSRRLPKGYKHLKDPILPGEIFKYMTVTEGDP 540  
541 TKSDDRCILFRYSSFYVMERDLASGLIGPLILCKESVDRGQMSDRNVILFSVDE 600  
541 TKSDDRCILFRYSSFYVMERDLASGLIGPLILCKESVDRGQMSDRNVILFSVDE 600  
601 NRSWYLTENIORFLPNPAGVOLEDEFOASINMSINGVFDLSQVCLAEVAYWYILS 660  
601 NRSWYLTENIORFLPNPAGVOLEDEFOASINMSINGVFDLSQVCLAEVAYWYILS 660  
661 IGAQNDPLSVFSGYTPFKHMYEDTLTFPFSGEYFVMSKMPGLMILGCHNSDFNRG 720  
661 IGAQNDPLSVFSGYTPFKHMYEDTLTFPFSGEYFVMSKMPGLMILGCHNSDFNRG 720  
721 MRLALKVSSCKNGDYEDSYEDLSAYLSKNNALTPRSFONSHPSTOKOPNATTI 780  
721 MRLALKVSSCKNGDYEDSYEDLSAYLSKNNALTPRSFONSHPSTOKOPNATTI 780  
781 PENDIEKTDPMFAHRTMPKTIQNVSSDLMLRQSPTPHGLSLDQAKYTFSDPS 840  
781 PENDIEKTDPMFAHRTMPKTIQNVSSDLMLRQSPTPHGLSLDQAKYTFSDPS 840  
841 PGALDSNNSLSEMTHFPPOLJHSGDMVFTPSGQLRLNKLQTTAATLKLDFKVSST 900  
841 PGALDSNNSLSEMTHFPPOLJHSGDMVFTPSGQLRLNKLQTTAATLKLDFKVSST 900  
901 SNNLSTIPSNLAAQDNTSSIGPPSPVHYDQDLDTLFGKSSPLTESGCLPISSEE 960  
901 SNNLSTIPSNLAAQDNTSSIGPPSPVHYDQDLDTLFGKSSPLTESGCLPISSEE 960  
961 NNDKYLSSGLMNSOESGMKNVSSGRLPFKRRHAGGALLTDMNLEFVYSTLKTN 1020  
961 NNDKYLSSGLMNSOESGMKNVSSGRLPFKRRHAGGALLTDMNLEFVYSTLKTN 1020  
1021 KTSNNSATNRKTHIDGSLTIENSPPVQNTLESDETFKKVPTLIDRLMDKNAALRL 1080  
1021 KTSNNSATNRKTHIDGSLTIENSPPVQNTLESDETFKKVPTLIDRLMDKNAALRL 1080  
1081 NMSKNTTSSKKNEMVQOKKEGPIPPDAQNDMSFFKMLFLPSARAWIQRTHGKNSLNSG 1140  
1081 NMSKNTTSSKKNEMVQOKKEGPIPPDAQNDMSFFKMLFLPSARAWIQRTHGKNSLNSG 1140  
1141 QGSPRKQVLSIGPEKSVYEQGNFLSEKKNVYVKGKEFTKVDGLKEMVFPSSRNLFLLTMDN 1200  
1141 QGSPRKQVLSIGPEKSVYEQGNFLSEKKNVYVKGKEFTKVDGLKEMVFPSSRNLFLLTMDN 1200

Qy	1201	LHNNTHNOEKKIOEBIEKKETLLOENVVLPJHITVTGKNPMKNLFIILSTRONVEGSYD	1260
Db	1201	LHNNTHNOEKKIOEBIEKKETLLOENVVLPJHITVTGKNPMKNLFIILSTRONVEGSYD	1260
Qy	1261	GAYAPVLQDFRSINDNTNKKHTAHFSKGEENEGIGNOTKQIVKACCTTRISPMPT	1320
Db	1261	GAYAPVLQDFRSINDNTNKKHTAHFSKGEENEGIGNOTKQIVKACCTTRISPMPT	1320
Qy	1321	SOQNFVYQBSKRALKQFLPLEETLEKRIIVDTSTQSKMKMLTPSTLTQIDINEKE	1380
Db	1321	SOQNFVYQBSKRALKQFLPLEETLEKRIIVDTSTQSKMKMLTPSTLTQIDINEKE	1380
Qy	1381	KGAITOSPLSDCLTRSHSIPQANRSPPLIAKVSFSPSIRPLYTRVLEFODNSHLPAA5	1440
Db	1381	KGAITOSPLSDCLTRSHSIPQANRSPPLIAKVSFSPSIRPLYTRVLEFODNSHLPAA5	1440
Qy	1441	RKDSGVQESSHFLQAKKNLSLAILTLEMTGDQREVGSLGTSATNSVYKKRENTVLP	1500
Db	1441	RKDSGVQESSHFLQAKKNLSLAILTLEMTGDQREVGSLGTSATNSVYKKRENTVLP	1500
Qy	1501	KPOLPKTSGVLELLPKVHTYOKDLPPRETSNGSPGHLDBEGSLLOGTREGAKMNEANRP	1560
Db	1501	KPOLPKTSGVLELLPKVHTYOKDLPPRETSNGSPGHLDBEGSLLOGTREGAKMNEANRP	1560
Qy	1561	GVPPPLRVATESSAKTPSKLDLPLAMDNHVGTOIPKEENKSOEKSPEKTAERKKDITLSL	1620
Db	1561	GVPPPLRVATESSAKTPSKLDLPLAMDNHVGTOIPKEENKSOEKSPEKTAERKKDITLSL	1620
Qy	1621	NACSNHAIIAINEGONKPEIEVTWAKOGFTEERLCSQNPVYLKRHOREITRTTLOSDOE	1680
Db	1621	NACSNHAIIAINEGONKPEIEVTWAKOGFTEERLCSQNPVYLKRHOREITRTTLOSDOE	1680
Qy	1681	IDYDQTSIVEMKKEDDIDYDEENOSPRSFOKTRHRYFAAVERLMDYGMSSPHYLARN	1740
Db	1681	IDYDQTSIVEMKKEDDIDYDEENOSPRSFOKTRHRYFAAVERLMDYGMSSPHYLARN	1740
Qy	1741	AOSGSVPQKKVYFOEFTGSGFTQPLRYGELNHEHLGLPTRYRAVEENTIMVTRQASR	1800
Db	1741	AOSGSVPQKKVYFOEFTGSGFTQPLRYGELNHEHLGLPTRYRAVEENTIMVTRQASR	1800
Qy	1801	PYSFYSLLISYEEBDOQGAEPKRNFKVNETKTYFMKVQHNAAPKDEFDCKAMAVFSDV	1860
Db	1801	PYSFYSLLISYEEBDOQGAEPKRNFKVNETKTYFMKVQHNAAPKDEFDCKAMAVFSDV	1860
Qy	1861	DLEKDVHSGLICPLVCHTNTLNPAGROVYVQEFALFTIPDETFSKYFTENNERCRA	1920
Db	1861	DLEKDVHSGLICPLVCHTNTLNPAGROVYVQEFALFTIPDETFSKYFTENNERCRA	1920
Qy	1921	PCNIOMEDPTFKENYFHAINGYIMDTLPGLVMAOORIRMYLLSMGSNEMIHSHFSGH	1980
Db	1921	PCNIOMEDPTFKENYFHAINGYIMDTLPGLVMAOORIRMYLLSMGSNEMIHSHFSGH	1980
Qy	1981	VFTYRKKKEETKALYLYGVEFEVEMLPKAKGIMRVECLIGBHLHAGMSTLFLVSNKC	2040
Db	1981	VFTYRKKKEETKALYLYGVEFEVEMLPKAKGIMRVECLIGBHLHAGMSTLFLVSNKC	2040
Qy	2041	QTPLGMA5GHIIRDFOITASGOYGOWAPKRLAHLHSGSINAMSTKPEFSMIVDLAPMI	2100
Db	2041	QTPLGMA5GHIIRDFOITASGOYGOWAPKRLAHLHSGSINAMSTKPEFSMIVDLAPMI	2100
Qy	2101	HGKTQGAORQFSSSLYISOFIIMYSLDGKKQYRGNGSTGLIMVFQVDSGSKKHIFW	2160
Db	2101	HGKTQGAORQFSSSLYISOFIIMYSLDGKKQYRGNGSTGLIMVFQVDSGSKKHIFW	2160
Qy	2161	PTIARIYRIHLPHYHSIRSTLHMLMGCDLNSGMPLGMSKRAISDAOTTSSTFTMFA	2220
Db	2161	PTIARIYRIHLPHYHSIRSTLHMLMGCDLNSGMPLGMSKRAISDAOTTSSTFTMFA	2220
Qy	2221	TWSPSKARLHLQGSNAARPOVNNPKEMLQVDFQKTKYTGVTGQVBSLTSYVKEFL	2280
Db	2221	TWSPSKARLHLQGSNAARPOVNNPKEMLQVDFQKTKYTGVTGQVBSLTSYVKEFL	2280

Qy	2281	ISSODGHOWTLFFONGKVKVQGNDSFTPVVNSIDPPLTRYLRIHPOSWHOIALRM	2340
Db	2281	ISSODGHOWTLFFONGKVKVQGNDSFTPVVNSIDPPLTRYLRIHPOSWHOIALRM	2340
Qy	2341	EVLGCEAODLY 2351	
Db	2341	EVLGCEAODLY 2351	

  

Qy	1	MOELSTCFPLCLLRPCFSATRRYVIGAVELSDWYQSDGLPELPVDARPPRPVKSFPFN	60
Db	1	MOELSTCFPLCLLRPCFSATRRYVIGAVELSDWYQSDGLPELPVDARPPRPVKSFPFN	60

QY	61	TSVYKKTLFVEPTHLEFNIAKPRPPMGLGPTIOAEYDYNVYTLKNASHPSLHAY	120
Db	61	TSVYKKTLFVEPTHLEFNIAKPRPPMGLGPTIOAEYDYNVYTLKNASHPSLHAY	120
QY	121	GVSTWKASBEGAYDDOTSOREKEDKYFPGSGHTYVWOVLKENGMA5DPLCLTYSYLSH	180
Db	121	GVSTWKASBEGAYDDOTSOREKEDKYFPGSGHTYVWOVLKENGMA5DPLCLTYSYLSH	180
QY	181	VDLVKDLNSGLIGALLVYREGSLAKERTQTLHFFILFVFEDEGKSHSEKNSLMQDD	240
Db	181	VDLVKDLNSGLIGALLVYREGSLAKERTQTLHFFILFVFEDEGKSHSEKNSLMQDD	240
QY	241	AASARAMPKMHYNGVNRSLPGLIGCHRSYVWHYIGMGTPEVHSLFEGHTFLYRNH	300
Db	241	AASARAMPKMHYNGVNRSLPGLIGCHRSYVWHYIGMGTPEVHSLFEGHTFLYRNH	300
QY	301	ROASLEISPTTFLTAOTLLMDLGOFLFCHISSHOHGMEAYVKVDSOPEPOLRKNNE	360
Db	301	ROASLEISPTTFLTAOTLLMDLGOFLFCHISSHOHGMEAYVKVDSOPEPOLRKNNE	360
QY	361	EAEDYDDLTDSEMDVYRFDDNSPSFTQIRSAKKHPTWVHYIAAEEEDMDYALVLA	420
Db	361	EAEDYDDLTDSEMDVYRFDDNSPSFTQIRSAKKHPTWVHYIAAEEEDMDYALVLA	420
QY	421	PDDRSYSOYLNGPORIGRKYKKVYRMATDEFTKREALOIHESGILGPLYGEGDTL	480
Db	421	PDDRSYSOYLNGPORIGRKYKKVYRMATDEFTKREALOIHESGILGPLYGEGDTL	480
QY	481	LIFKNOASRPVNIYHGTIDYRPLYSRRLPKVAKHLKDFPLIGELFKKMYVEDOP	540
Db	481	LIFKNOASRPVNIYHGTIDYRPLYSRRLPKVAKHLKDFPLIGELFKKMYVEDOP	540
QY	541	TKSDPCLTRYSSFYNNERDLASGLIGPLLCYKESVDORONOTMSDKRNVILFSEDE	600
Db	541	TKSDPCLTRYSSFYNNERDLASGLIGPLLCYKESVDORONOTMSDKRNVILFSEDE	600
QY	601	NRSWYLTENIOFLPMPAGVOLDEPFOASINMHSINGVPSLOLSVCLHEVAYVYILS	660
Db	601	NRSWYLTENIOFLPMPAGVOLDEPFOASINMHSINGVPSLOLSVCLHEVAYVYILS	660
QY	661	IGAOTDFLSVFSGYTFKHKMYEDTLPLPFSGEYVFMSPMNGMLILCHNSDPRNG	720
Db	661	IGAOTDFLSVFSGYTFKHKMYEDTLPLPFSGEYVFMSPMNGMLILCHNSDPRNG	720
QY	721	MTALLKYSODCKMGTGYEDSYEDISAYLSKKNALIEPSSONSRRPSTRKOQFNAATT	780
Db	721	MTALLKYSODCKMGTGYEDSYEDISAYLSKKNALIEPSSONSRRPSTRKOQFNAATT	780
QY	781	PENDIEKTDPMFAHRTPMKIQONVSSDLMILKROSPPHGLISDLQEAKEYTFSDDS	840
Db	781	PENDIEKTDPMFAHRTPMKIQONVSSDLMILKROSPPHGLISDLQEAKEYTFSDDS	840
QY	841	PGALDSNNLSSEWTHRPOLHHSGDWFTPEGLOLRLENEKIGTTAATELKIDFVYSST	900
Db	841	PGALDSNNLSSEWTHRPOLHHSGDWFTPEGLOLRLENEKIGTTAATELKIDFVYSST	900
QY	901	SNNLISITIPSDNLAAGTNTSSIGPSPMYHYNSOJLTIGKXSSPLTSSGGPLSLSE	960
Db	901	SNNLISITIPSDNLAAGTNTSSIGPSPMYHYNSOJLTIGKXSSPLTSSGGPLSLSE	960
QY	961	NNSDKLLESGLMNSOESSMGKNVSTESGRLFGRKRAHGPALTRKDNALFKVYSISLKTN	1020
Db	961	NNSDKLLESGLMNSOESSMGKNVSTESGRLFGRKRAHGPALTRKDNALFKVYSISLKTN	1020
QY	1021	KTSNNSATNRKTHIDOPSLLIENSPLYWONILSDTEEFKKTYPPLIHRMLMDNATALE	1080
Db	1021	KTSNNSATNRKTHIDOPSLLIENSPLYWONILSDTEEFKKTYPPLIHRMLMDNATALE	1080
QY	1081	NHMSNKTTSKKNMEVWOKKEGPIPPDAONPDMSFPKMLFIPESARVNIORTHKNSLNG	1140
Db	1081	NHMSNKTTSKKNMEVWOKKEGPIPPDAONPDMSFPKMLFIPESARVNIORTHKNSLNG	1140
QY	1141	QGPSPKOLVSLGPEKSVBEGONFLSEKKNVYVVGGEFTKDVGLKEKMFPPSSRNLFITNLDN	1200
Db	1141	QGPSPKOLVSLGPEKSVBEGONFLSEKKNVYVVGGEFTKDVGLKEKMFPPSSRNLFITNLDN	1200
QY	1201	LHENNTNHOEKKIOEIEKKEPLLIOENVVLPQIHTVGTJNPKKNLFLSTRQNVESYD	1260
Db	1201	LHENNTNHOEKKIOEIEKKEPLLIOENVVLPQIHTVGTJNPKKNLFLSTRQNVESYD	1260
QY	1261	GAYAPVLOFBSLNDSTNRTKHTAHFSKKEEENLGLGNQKOIYERACTRISFNT	1320
Db	1261	GAYAPVLOFBSLNDSTNRTKHTAHFSKKEEENLGLGNQKOIYERACTRISFNT	1320
QY	1321	SOONFYTORSKRALKOPRLPEETELEKRTIYDDPTOSWKNKHLPTSTLOIDYNKE	1380
Db	1321	SOONFYTORSKRALKOPRLPEETELEKRTIYDDPTOSWKNKHLPTSTLOIDYNKE	1380
QY	1381	KGATIOSPLSDCLTRSHSIPQANRSPPLAKVSSPSTIRPYLTRVLFODNSSHLPAASY	1440
Db	1381	KGATIOSPLSDCLTRSHSIPQANRSPPLAKVSSPSTIRPYLTRVLFODNSSHLPAASY	1440
QY	1441	RKDSGVCESSHFLQGAKKNNLSIALITLLEMTGDQREVSGIGTSATNSVYKYKENTYLP	1500
Db	1441	RKDSGVCESSHFLQGAKKNNLSIALITLLEMTGDQREVSGIGTSATNSVYKYKENTYLP	1500
QY	1501	KDLPKTSQKVELLPKYHIYORDLPPTESNPGHLDVEGSLQGTGALTKMNEANRP	1560
Db	1501	KDLPKTSQKVELLPKYHIYORDLPPTESNPGHLDVEGSLQGTGALTKMNEANRP	1560
QY	1561	GVYPLRVATSSAKTSKLLDLANDNHYGOTPKREMKSOEKSEKTAFFKKDTLSL	1620
Db	1561	GVYPLRVATSSAKTSKLLDLANDNHYGOTPKREMKSOEKSEKTAFFKKDTLSL	1620
QY	1621	NACESNHAIAMINBOQKPEIEVYTWAKOGRTERLCSONPVYLRKHOREITRTTQSDOE	1680
Db	1621	NACESNHAIAMINBOQKPEIEVYTWAKOGRTERLCSONPVYLRKHOREITRTTQSDOE	1680
QY	1681	IDYDDPTISYEMKKEDPFIYDEDENOSPRSFOKTRHYFIAVERLDYGMSSSPHYLRNR	1740
Db	1681	IDYDDPTISYEMKKEDPFIYDEDENOSPRSFOKTRHYFIAVERLDYGMSSSPHYLRNR	1740
QY	1741	AQSGSVPOGKKVYFOEPTDGSFPQYLRCELNEHLGLGPLYIAEVEDIMVTFEQAQR	1800
Db	1741	AQSGSVPOGKKVYFOEPTDGSFPQYLRCELNEHLGLGPLYIAEVEDIMVTFEQAQR	1800
QY	1801	PYSFYSLLISYEEDROGABPRKNFAPKREKTAFFKVOHMMAPTRDEPDCKAAYFSDV	1860
Db	1801	PYSFYSLLISYEEDROGABPRKNFAPKREKTAFFKVOHMMAPTRDEPDCKAAYFSDV	1860
QY	1861	DLEKDVHSGLIGPLVCHTNTLPAHAGOVYVQEFALFTTIDETKSWYFTEENNERCRA	1920
Db	1861	DLEKDVHSGLIGPLVCHTNTLPAHAGOVYVQEFALFTTIDETKSWYFTEENNERCRA	1920
QY	1921	PCNIQWEDPTEKENYRFAHANGYIMDTLEGLVMAQODRIMNYLLSGNSNENHSHIFSCH	1980
Db	1921	PCNIQWEDPTEKENYRFAHANGYIMDTLEGLVMAQODRIMNYLLSGNSNENHSHIFSCH	1980
QY	1981	VFTYVRKKEEYKMALYXNYXPGVFETVYMLPSAAGIMRRECLIGHILAGMSTFLYVNSKC	2040
Db	1981	VFTYVRKKEEYKMALYXNYXPGVFETVYMLPSAAGIMRRECLIGHILAGMSTFLYVNSKC	2040
QY	2041	QYPLGMA5GHRDPOITASGOYQWAPKLARLHYSISINAMSTKEPFSITKYDLAPMTI	2100
Db	2041	QYPLGMA5GHRDPOITASGOYQWAPKLARLHYSISINAMSTKEPFSITKYDLAPMTI	2100
QY	2101	HGKTQGAOKOFSSLYTSOFTIYSLDGKKQYQTRGNSGTTLVWFPGVNDSSGJKHNTFN	2160
Db	2101	HGKTQGAOKOFSSLYTSOFTIYSLDGKKQYQTRGNSGTTLVWFPGVNDSSGJKHNTFN	2160
QY	2161	PLIARVYLRPHYTSJRSRTLREMLGCDLNSCNPJGMSKSAISPAOTIASSYFTNMFA	2220
Db	2161	PLIARVYLRPHYTSJRSRTLREMLGCDLNSCNPJGMSKSAISPAOTIASSYFTNMFA	2220
QY	2221	TMSPSKARLHLOGNSNMPOVNNKPEMLQVDFOKYTKVGTVQGVASLTSMTYVEFL	2280
Db	2221	TMSPSKARLHLOGNSNMPOVNNKPEMLQVDFOKYTKVGTVQGVASLTSMTYVEFL	2280

Db 2221 TWSPSKARLLHLOGKSNANRPVNPKEMLQVDFOKTMKVTGQVSLTSMVYKEFL 2280  
QY 2281 ISSSDGQHOWTLFQNGKVKVFGQNDSPFPVNVSLDPLRLTRYLRKTRHPSWVHQIALRM 2340  
|||||  
Db 2281 ISSSDGQHOWTLFQNGKVKVFGQNDSPFPVNVSLDPLRLTRYLRKTRHPSWVHQIALRM 2340  
|||||  
QY 2341 EVLGCENADLY 2351  
|||||  
Db 2341 EVLGCENADLY 2351  
|||||  
RESULT 5  
AA52537  
ID AA52537 standard: Protein: 2351 AA.  
AC AA52537;  
XX  
DT 28-FEB-2000 (first entry)  
XX  
DE Human full-length factor VIII.  
XX  
KM Factor VIII: haemophilia; proteolysis; heavy chain; light chain;  
KM secretion: von Willebrand factor; VWF; C2 domain; intron 22; inversion;  
KM non-functional; bleeding disorder; coagulation; treatment.  
XX  
OS Homo sapiens.  
XX  
FH Key Location/Qualifiers  
FT Peptide 1..19  
FT /note= "Signal peptide"  
FT Protein 20..1708  
FT /note= "Maximum length human factor VIII heavy chain"  
FT Protein 1709..2351  
FT /note= "Human factor VIII light chain"  
XX  
PN MO9959622-A1.  
XX  
PD 25-NOV-1999.  
XX  
PE 17-MAY-1999; 99MO-US10872.  
XX  
PR 20-MAY-1998; 9805-0082000.  
XX  
PA (GETH ) GENENTECH INC.  
XX  
PI Vohar GA;  
XX  
DR WPI: 2000-053195/04.  
DR N-PSDB: AA238604.  
XX  
PT New method for treating hemophilia A -  
XX  
PS Disclosure: Fig 9; 50pp: English.  
XX  
CC This sequence represents the full-length human factor VIII. In  
CC this form, the protein is 300 kD in size with the domain structure  
CC A1-A2-B-A3-C1-C2. However, prior to secretion, this 300 kD protein  
CC is proteolysed into a heavy chain (A1-A2-B, with continued  
CC proteolysis within the B domain resulting in molecules of varying  
CC length) and a light chain (A3-C1-C2) that remains non-covalently attached  
CC to the heavy chain. Upon secretion, factor VIII is rapidly cleared from  
CC the circulation unless it is bound by the plasma protein von Willebrand  
CC Factor (VWF). Factor VIII binds to VWF through the light chain, with  
CC known binding sites at the N-terminus and within the C2 domain.  
CC Haemophilia A is frequently caused by an intron 22 inversion in the  
CC factor VIII gene, which separates the gene into two sections, exons 1-22  
CC becoming inverted and localised telomeric to the original site, while  
CC exons 23-26 remain isolated at the original site. Exons 23-26 a portion  
CC of the C1 and all of the C2 domains, without which factor VIII is  
CC non-functional. The factor VIII gene product of individuals with this  
CC mutation thus comprises domains A1-A2-B-A3 plus a fragment of C1, which  
CC on proteolysis is non-functional, resulting in a bleeding disorder. The  
CC invention relates to a novel method for for treating haemophilia A in a

CC mammal able to produce the factor VIII heavy chain. The method comprises  
CC administering to the mammal either an effective amount of factor VIII  
CC light chain, or a gene encoding it, and may be useful for treating  
CC patients such as those whose haemophilia A is caused by intron 22  
CC inversion. The recombinant factor VIII products of this invention are  
CC derived from well-characterised starting materials which therefore  
CC reduces the risk of pathogenic infection which was previously a problem  
CC when using donated plasma. Furthermore, the invention provides a more  
CC economic and potentially more effective treatment for haemophilia. There  
CC is also a need of providing factor VIII activity to patients who  
CC produce or are at risk of producing antibodies against full-length  
CC factor VIII.  
XX  
SQ Sequence 2351 AA:  
Query Match 100.0%; Score 12418; DB 21; Length 2351;  
Best Local Similarity 100.0%; Pred. NO. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 0; Gaps 0;  
QY 1 MQETLSTCFCLLRFCFSATRRYLGAVELSMYQMSDGLPVDARPPVPKSPFN 60  
Db 1 MQETLSTCFCLLRFCFSATRRYLGAVELSMYQMSDGLPVDARPPVPKSPFN 60  
QY 61 TSYVYKKTLPVEFDHLEFNIAKRPWMGLDPTIOAVYDVTVITLKMASHPSIAV 120  
Db 61 TSYVYKKTLPVEFDHLEFNIAKRPWMGLDPTIOAVYDVTVITLKMASHPSIAV 120  
QY 121 GVSYWKASGAEYDDYTSOREKEDDKVFPGSHYVWQVLEKGNPASDPLCLTVSYLSH 180  
Db 121 GVSYWKASGAEYDDYTSOREKEDDKVFPGSHYVWQVLEKGNPASDPLCLTVSYLSH 180  
QY 181 VDLVKDNLGSLGALLVCBQSLAKKKTOTLAKFLLFAVDEGKSMHSEFNLSLMQORD 240  
Db 181 VDLVKDNLGSLGALLVCBQSLAKKKTOTLAKFLLFAVDEGKSMHSEFNLSLMQORD 240  
QY 241 AASARAPMKHNTVYNGVYNRSLDLCGHKSYVMYVIGMTGPVYSTLGEHTLVNHN 300  
Db 241 AASARAPMKHNTVYNGVYNRSLDLCGHKSYVMYVIGMTGPVYSTLGEHTLVNHN 300  
QY 301 RQASLEISPTFLTAQTLMDLQOFLFCHISSHODGMEAYKVDSCPEBOLMKKNE 360  
Db 301 RQASLEISPTFLTAQTLMDLQOFLFCHISSHODGMEAYKVDSCPEBOLMKKNE 360  
QY 361 EADYVDLDTLSEMDVYRFDODNSPSFIOIRSVAKKHKTVMHYIAAEEEDMDVPLVA 420  
Db 361 EADYVDLDTLSEMDVYRFDODNSPSFIOIRSVAKKHKTVMHYIAAEEEDMDVPLVA 420  
QY 421 PDDRKYKSOYLNNGPORIGRKVKYKPMAYTEPEKTRZEAIOHESGILGPLXGEGVDTL 480  
Db 421 PDDRKYKSOYLNNGPORIGRKVKYKPMAYTEPEKTRZEAIOHESGILGPLXGEGVDTL 480  
QY 481 LITFKNQASRPYNTYPHGITDVRPLYSRLPRGVNHLKDPILBGEIFKYKMTVVEDGP 540  
Db 481 LITFKNQASRPYNTYPHGITDVRPLYSRLPRGVNHLKDPILBGEIFKYKMTVVEDGP 540  
QY 541 TKSDPRLCTRRYSSVFWMERDLASGLIGPLLCYKESVDQNGQINSDKRNVIILSVDE 600  
Db 541 TKSDPRLCTRRYSSVFWMERDLASGLIGPLLCYKESVDQNGQINSDKRNVIILSVDE 600  
QY 601 NRSWYLTENIOFLPNPAGVOLDEPEFQSNIMHSINGVDSLOISVCHVAVWYLS 660  
Db 601 NRSWYLTENIOFLPNPAGVOLDEPEFQSNIMHSINGVDSLOISVCHVAVWYLS 660  
QY 661 IGAQOTPLSVFSGYTKRHKMYEDTLTFPPSGGTVKSNENRGMLTGCNNSPFRNG 720  
Db 661 IGAQOTPLSVFSGYTKRHKMYEDTLTFPPSGGTVKSNENRGMLTGCNNSPFRNG 720  
QY 721 MTALLKVVSSCDKNQGYEDSYEDISAVLLSKNNAIEBRPSQNSRHPSTROKOPNATTI 780  
Db 721 MTALLKVVSSCDKNQGYEDSYEDISAVLLSKNNAIEBRPSQNSRHPSTROKOPNATTI 780  
QY 781 PENDIKTQPMFAHHTPMPKIQOVSSDLMILRQSPPHGLSLDQAKKETSDPS 840  
Db 781 PENDIKTQPMFAHHTPMPKIQOVSSDLMILRQSPPHGLSLDQAKKETSDPS 840

Db 781 PENDIEKTDPMFAHRTMPKIQNVSSSDLLMLRQSPTRPGLSLSDIQEAKYETPDDPS 840  
Qy 841 PGADISNNSISEMTHPPOHLSHSGDVFPPESGIOLRLNKEKLTATATLKKLDDKVSST 900  
Db 841 PGADISNNSISEMTHPPOHLSHSGDVFPPESGIOLRLNKEKLTATATLKKLDDKVSST 900  
Qy 901 SNNLSTIPSDNLAAGTDNNTSSLGPPSMFVHDQDITTLTGKXSSPILDESGPILSEE 960  
Db 901 SNNLSTIPSDNLAAGTDNNTSSLGPPSMFVHDQDITTLTGKXSSPILDESGPILSEE 960  
Qy 961 NNDKSLLEGLMNSOESSSMGKNVSTESGRLEKGRAGHPALLTKNALFKVYSILKTN 1020  
Db 961 NNDKSLLEGLMNSOESSSMGKNVSTESGRLEKGRAGHPALLTKNALFKVYSILKTN 1020  
Qy 1021 KTSNNSATNRKTHIDGSLILENSPVMONILESTDEPKKVTPLIDHRLMOMKNATLRL 1080  
Db 1021 KTSNNSATNRKTHIDGSLILENSPVMONILESTDEPKKVTPLIDHRLMOMKNATLRL 1080  
Qy 1081 NMSKNTTSSKNMEXQCKEGPIPDADONPMSFFKMLFPESARWIOETGKXSLNSG 1140  
Db 1081 NMSKNTTSSKNMEXQCKEGPIPDADONPMSFFKMLFPESARWIOETGKXSLNSG 1140  
Qy 1141 QGSPKQIYSLGPEKSYEGONFLSEKNKYVVGKGEFTKDVLKEMVFPSSRLFTLNLDN 1200  
Db 1141 QGSPKQIYSLGPEKSYEGONFLSEKNKYVVGKGEFTKDVLKEMVFPSSRLFTLNLDN 1200  
Qy 1201 LHENNTNHOEKKIOEIEIEKKEKTLIOENVYLPIHTVTGKXPMKNFLISTRONVSGSD 1260  
Db 1201 LHENNTNHOEKKIOEIEIEKKEKTLIOENVYLPIHTVTGKXPMKNFLISTRONVSGSD 1260  
Qy 1261 GATAPVLODFRSLDNSTNRKTKTAHFSKKGEBNLEGLQOTQIYEKACTRISPT 1320  
Db 1261 GATAPVLODFRSLDNSTNRKTKTAHFSKKGEBNLEGLQOTQIYEKACTRISPT 1320  
Qy 1321 SOONFVTOXRKRALQKQRLPLEETELEKRIYVDITSTOMSKNMKHLPTLTQIDYNEKE 1380  
Db 1321 SOONFVTOXRKRALQKQRLPLEETELEKRIYVDITSTOMSKNMKHLPTLTQIDYNEKE 1380  
Qy 1381 KGATOSPPLSDCLTSHSIPQANSPPLPAKXSSPPIRYLFRVLFQDNSSHLPAASY 1440  
Db 1381 KGATOSPPLSDCLTSHSIPQANSPPLPAKXSSPPIRYLFRVLFQDNSSHLPAASY 1440  
Qy 1441 RKDSCVOSSHFDGAKAKNNLSALITILEMGDQREVGSLGTSATNSYKKVENTYLP 1500  
Db 1441 RKDSCVOSSHFDGAKAKNNLSALITILEMGDQREVGSLGTSATNSYKKVENTYLP 1500  
Qy 1501 KPDLPTSGKVELLPKVAHYOKDLEPTETSNGSPGHLDLVGSLLQSTEGALIKWNEANRP 1560  
Db 1501 KPDLPTSGKVELLPKVAHYOKDLEPTETSNGSPGHLDLVGSLLQSTEGALIKWNEANRP 1560  
Qy 1561 GKVPLRVATESSASPTSKLIDPLAMDNHYGQIPIKEEMKSOEKSPEKTAFFKKKDTILSL 1620  
Db 1561 GKVPLRVATESSASPTSKLIDPLAMDNHYGQIPIKEEMKSOEKSPEKTAFFKKKDTILSL 1620  
Qy 1621 NACESNHAIATINEQONPEIEVYMAKOGTEKLSQNPVYLKHOREITRTLOSDOE 1680  
Db 1621 NACESNHAIATINEQONPEIEVYMAKOGTEKLSQNPVYLKHOREITRTLOSDOE 1680  
Qy 1681 IDYDDTISVEMKKEDEFDIYDENQSPRSFOKTRHYFLAAVERLMDYGSSSPHVLNR 1740  
Db 1681 IDYDDTISVEMKKEDEFDIYDENQSPRSFOKTRHYFLAAVERLMDYGSSSPHVLNR 1740  
Qy 1741 AOGSGVPOFKKVPVPOEFDGSEFOTPLRGELNHLGILGPYIRAEVEDNIMVFRNOQR 1800  
Db 1741 AOGSGVPOFKKVPVPOEFDGSEFOTPLRGELNHLGILGPYIRAEVEDNIMVFRNOQR 1800  
Qy 1801 PYSFYSSLISYEDDROGAEPKRNKVPNETKTYFKVQVHMAEPKDEPCKKAAVFSY 1860  
Db 1801 PYSFYSSLISYEDDROGAEPKRNKVPNETKTYFKVQVHMAEPKDEPCKKAAVFSY 1860  
Qy 1861 DLEKDVHSGILGPLVCHTNTLNPAHGRQVTVQEFALFTTIFDETCKMYFTENNERCRA 1920  
Db 1861 DLEKDVHSGILGPLVCHTNTLNPAHGRQVTVQEFALFTTIFDETCKMYFTENNERCRA 1920

Qy 1921 PCNIQMEDPTREKENYRPHAINGYINDTLPGLVMAODORIIMWLLSGNSENIHISGSH 1980  
Db 1921 PCNIQMEDPTREKENYRPHAINGYINDTLPGLVMAODORIIMWLLSGNSENIHISGSH 1980  
Qy 1981 VFTYARKKEEYKMAIYNLYGVEFETVEMLSKAGIMRWRECLIGEHJAGKSTLFLVYSNKC 2040  
Db 1981 VFTYARKKEEYKMAIYNLYGVEFETVEMLSKAGIMRWRECLIGEHJAGKSTLFLVYSNKC 2040  
Qy 2041 QTPDGMASGHRDFOQTASQIGQVNAKPLALHSGSINMSTKEPFSYIVDLAPMI 2100  
Db 2041 QTPDGMASGHRDFOQTASQIGQVNAKPLALHSGSINMSTKEPFSYIVDLAPMI 2100  
Qy 2101 HGKITOGAROKFSSLYISOFIIMYSLSDKKKQOTYRGNSTGTLWVFEGVDSGILKHINFN 2160  
Db 2101 HGKITOGAROKFSSLYISOFIIMYSLSDKKKQOTYRGNSTGTLWVFEGVDSGILKHINFN 2160  
Qy 2161 PPLIARYLRILHPHYSTRSTLRMELMGCDLNSCMPLGMSKASIDAOITASVFTNMFA 2220  
Db 2161 PPLIARYLRILHPHYSTRSTLRMELMGCDLNSCMPLGMSKASIDAOITASVFTNMFA 2220  
Qy 2221 TWSPSKARLHIOGRSNAMRPQVANNKPEMLQVDFOKTKKVTGTOGYSILITSMYREFL 2280  
Db 2221 TWSPSKARLHIOGRSNAMRPQVANNKPEMLQVDFOKTKKVTGTOGYSILITSMYREFL 2280  
Qy 2281 ISSSDQGHQWTLFPQNGKRVFQGNDSFTPVVNSLDPLLTTRYLRIRHQSVMHOIALRM 2340  
Db 2281 ISSSDQGHQWTLFPQNGKRVFQGNDSFTPVVNSLDPLLTTRYLRIRHQSVMHOIALRM 2340  
Qy 2341 EYLIGCEADDL 2351  
Db 2341 EYLIGCEADDL 2351  
RESULT 6  
AAM11435  
ID AAM11435 standard; Protein: 2351 AA.  
XX  
XX AAM11435;  
DT 20-NOV-1997 (first entry)  
XX  
DE Active Factor VIII:C analogue S1311X.  
XX  
XX Factor VIII:C: analogue; glycoprotein; blood coagulation cascade;  
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KW plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;  
KW proteolytic cleavage.  
XX  
OS Homo sapiens.  
OS Synthetic.  
XX  
FH Key Location/Qualifiers  
FT Peptide 1..19  
FT Protein 20..2351  
FT Region /note="mature Factor VIII:C"  
FT 20..1667  
FT Modified-site /note="heavy chain fragment"  
FT 1330  
FT Region /label="pne, Glu, Pro  
FT 1668..2350  
FT Domain /note="light chain fragment"  
FT 760..1667  
FT /note="B domain"  
PN W09703195-A1.  
XX  
XX 30-JAN-1997.  
PD  
XX 09-JUL-1996; 96MO-US11444.  
PF  
XX 11-JUL-1995; 95US-0001025.

XX (CHIR ) CHIRON CORP.  
XX  
PI Cohen FE, Hung DT, Innis M;  
XX WPI; 1997-119050/11.  
XX  
XX Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophilias, by improvement of  
PT haemostasis  
XX  
PS Claim 30; Page -: 90pp; English.  
XX  
CC AAM1330-W1472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAF51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophilias, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX  
XX  
SQ Sequence 2351 AA:  
  
Query Match 100.0%; Score 12414; DB 18; Length 2351;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2350; Conservative 0; Mismatches 0; Indels 0; Gaps 0;  
  
QY 1 MOELSTCFPLCLLRFCSATRRYYLGAVELSNDYMOSDGLGELPYDARPPRPVKSPPFN 60  
DB 1 MOELSTCFPLCLLRFCSATRRYYLGAVELSNDYMOSDGLGELPYDARPPRPVKSPPFN 60  
QY 61 TSVYKKTLFEVFTDHLFNIAPRPPMGLGPTIQAEVYDVYITLKNMASHPVSLHAV 120  
DB 61 TSVYKKTLFEVFTDHLFNIAPRPPMGLGPTIQAEVYDVYITLKNMASHPVSLHAV 120  
QY 121 GVSYWKASGAEVDDQTSOREKEDKVPFGSHYVMQVLKENGPMASDPLCYSLSH 180  
DB 121 GVSYWKASGAEVDDQTSOREKEDKVPFGSHYVMQVLKENGPMASDPLCYSLSH 180  
QY 121 GVSYWKASGAEVDDQTSOREKEDKVPFGSHYVMQVLKENGPMASDPLCYSLSH 180  
DB 121 GVSYWKASGAEVDDQTSOREKEDKVPFGSHYVMQVLKENGPMASDPLCYSLSH 180  
QY 181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLAKFILLFAVDEGKSMHSETKNSLMODRD 240  
DB 181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLAKFILLFAVDEGKSMHSETKNSLMODRD 240  
QY 181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLAKFILLFAVDEGKSMHSETKNSLMODRD 240  
DB 181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLAKFILLFAVDEGKSMHSETKNSLMODRD 240  
QY 241 AASARAMPKMHYNGVYVNSRLPGLICGRKSVYMHVIGMGTPEVHSIFLEGHFTLVNRH 300  
DB 241 AASARAMPKMHYNGVYVNSRLPGLICGRKSVYMHVIGMGTPEVHSIFLEGHFTLVNRH 300  
QY 241 AASARAMPKMHYNGVYVNSRLPGLICGRKSVYMHVIGMGTPEVHSIFLEGHFTLVNRH 300  
DB 241 AASARAMPKMHYNGVYVNSRLPGLICGRKSVYMHVIGMGTPEVHSIFLEGHFTLVNRH 300  
QY 301 RQASLEISPTFTLTAOTLLMDLGOFLFLCHSHQHDMGMAVYKXDSCEEPOLRMKNE 360  
DB 301 RQASLEISPTFTLTAOTLLMDLGOFLFLCHSHQHDMGMAVYKXDSCEEPOLRMKNE 360  
QY 301 RQASLEISPTFTLTAOTLLMDLGOFLFLCHSHQHDMGMAVYKXDSCEEPOLRMKNE 360  
DB 301 RQASLEISPTFTLTAOTLLMDLGOFLFLCHSHQHDMGMAVYKXDSCEEPOLRMKNE 360  
QY 361 EAEDYDDLTDSEMDVVRFDNDSPTQIRSVAKKHPTWVHYIAAEEDMDYAPLVLA 420  
DB 361 EAEDYDDLTDSEMDVVRFDNDSPTQIRSVAKKHPTWVHYIAAEEDMDYAPLVLA 420  
QY 361 EAEDYDDLTDSEMDVVRFDNDSPTQIRSVAKKHPTWVHYIAAEEDMDYAPLVLA 420  
DB 361 EAEDYDDLTDSEMDVVRFDNDSPTQIRSVAKKHPTWVHYIAAEEDMDYAPLVLA 420  
QY 421 PDDRSYSQYTLNNGPQRIGRKYKRYFMAAYTDEFKTRALIOHESGILGPLLGYGVDTL 480  
DB 421 PDDRSYSQYTLNNGPQRIGRKYKRYFMAAYTDEFKTRALIOHESGILGPLLGYGVDTL 480  
QY 421 PDDRSYSQYTLNNGPQRIGRKYKRYFMAAYTDEFKTRALIOHESGILGPLLGYGVDTL 480  
DB 421 PDDRSYSQYTLNNGPQRIGRKYKRYFMAAYTDEFKTRALIOHESGILGPLLGYGVDTL 480  
QY 481 LTIFFKQASRPYNIYHGHITDVRLYLSRRLPKGVKHLKDPILLGSEIFKRYKWTYVEDGP 540  
DB 481 LTIFFKQASRPYNIYHGHITDVRLYLSRRLPKGVKHLKDPILLGSEIFKRYKWTYVEDGP 540

DB 481 LTIFFKQASRPYNIYHGHITDVRLYLSRRLPKGVKHLKDPILLGSEIFKRYKWTYVEDGP 540  
QY 541 TRSDPCLTRYSSFFVNMERDLASLIGPLLCYKESVDQGNQMSKRVLLFSEVDE 600  
DB 541 TRSDPCLTRYSSFFVNMERDLASLIGPLLCYKESVDQGNQMSKRVLLFSEVDE 600  
QY 601 NRSWYLTENIÖRELPMNPAGVQLEDEBEFOASNIMHSINGVYFSDLOLVCLEHVAWYILS 660  
DB 601 NRSWYLTENIÖRELPMNPAGVQLEDEBEFOASNIMHSINGVYFSDLOLVCLEHVAWYILS 660  
QY 661 IGAÖDFLSYFESGYTFKRYKRYEDTLTFPFSGEYFVMSMEMPGLMILGCHNSDFFYNRG 720  
DB 661 IGAÖDFLSYFESGYTFKRYKRYEDTLTFPFSGEYFVMSMEMPGLMILGCHNSDFFYNRG 720  
QY 721 MTALLKVSQCDKNTGYEDSDIEDISAVLSKNNALIEPNSFSONSRHPSTQOPNATYI 780  
DB 721 MTALLKVSQCDKNTGYEDSDIEDISAVLSKNNALIEPNSFSONSRHPSTQOPNATYI 780  
QY 781 PENDIEKTDPMFAHRTPMKIONVSSDLMMLRÖSPTPHGLSLSDQAEYETFSDDPS 840  
DB 781 PENDIEKTDPMFAHRTPMKIONVSSDLMMLRÖSPTPHGLSLSDQAEYETFSDDPS 840  
QY 841 PGATDSNNLSSEKTHRRPOLHSGDMFTPSPGLOLALNKLGTAAETIKLDPFYVST 900  
DB 841 PGATDSNNLSSEKTHRRPOLHSGDMFTPSPGLOLALNKLGTAAETIKLDPFYVST 900  
QY 901 SNMLISTIPSDNLAAGTDNTSSLGPPSPVHYDSQDLDTLPGKSSPLTESGGPLSSEE 960  
DB 901 SNMLISTIPSDNLAAGTDNTSSLGPPSPVHYDSQDLDTLPGKSSPLTESGGPLSSEE 960  
QY 961 NNDKSLFESGIMNSÖSSMGKRVVSTESGRFLFKRKRAHGALLTKONALFYVSIILKTN 1020  
DB 961 NNDKSLFESGIMNSÖSSMGKRVVSTESGRFLFKRKRAHGALLTKONALFYVSIILKTN 1020  
QY 1021 KTSNNSATNKRKTHIDPSSLINSGSVQNLNLESDPEFKKVPRLIHDMILDKNATRL 1080  
DB 1021 KTSNNSATNKRKTHIDPSSLINSGSVQNLNLESDPEFKKVPRLIHDMILDKNATRL 1080  
QY 1081 NMSNKTTSKKNEMVQOKKEGPIPPDAQNDMSFFKMLFLPESARWIORHGNKNSLNG 1140  
DB 1081 NMSNKTTSKKNEMVQOKKEGPIPPDAQNDMSFFKMLFLPESARWIORHGNKNSLNG 1140  
QY 1141 QGSPKQOLVSLGPEKSEVQONFLSEKKNVYVVGKEEFLKDGLEKEMVFPSSRLFLTNLDN 1200  
DB 1141 QGSPKQOLVSLGPEKSEVQONFLSEKKNVYVVGKEEFLKDGLEKEMVFPSSRLFLTNLDN 1200  
QY 1201 LHENNTHÖEKKIOEIEIEKKEKTLIOENVVLQOHTVYGTNFKNLFLILSTRÖVBEQSYD 1260  
DB 1201 LHENNTHÖEKKIOEIEIEKKEKTLIOENVVLQOHTVYGTNFKNLFLILSTRÖVBEQSYD 1260  
QY 1261 GAYAVVLÖDERSLNDSTNRTKKHTAHFSKKEEENLEGLÖNÖTKOIVERYACTRISPT 1320  
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QY 1321 SQÖNFVTOQRKALQOFRLPLEETELERKRIIVDPTÖSÖMKNKHILTESLTQIDYNEKE 1380  
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QY 1381 KCATÖSPILSPCLTRSHSTIPÖANRSPFLIAYVSSFPIRPIYTLVTLÖDÖNDSHLPAASY 1440  
DB 1381 KCATÖSPILSPCLTRSHSTIPÖANRSPFLIAYVSSFPIRPIYTLVTLÖDÖNDSHLPAASY 1440  
QY 1441 RKÖDSGVOESSHFLÖGAKKNNLSLAILTLEMTGÖREVGSLGATSNSVYRKKEVNTLP 1500  
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QY 1501 KPDLPTKSGKVELLPKVHLYQKDLPPETSSNGSGHLDLVESGLÖGTGALKNMEANRP 1560  
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QY 1561 GAVPFLKATVSSAKTPSKLDPPLAMDWHYGTQIPREKMSQKSPKRTAKKKTLLSL 1620  
DB 1561 GAVPFLKATVSSAKTPSKLDPPLAMDWHYGTQIPREKMSQKSPKRTAKKKTLLSL 1620



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Db      1561  GKVPLFVATESSAKTPSKLDDPLAMDNHYGTQIPKEENKSOEKSPERTAFKKKDTLLSL 1620
Qy      1621  NACENHAIIAINEGONKPEIEVWAKQRTERLCSNPVLRKHQREITRTTLOSQOE 1680
Db      1621  NACENHAIIAINEGONKPEIEVWAKQRTERLCSNPVLRKHQREITRTTLOSQOE 1680
Qy      1681  IDYDDITSVMKKEDDIYDEDENSPSPKQRTTRHYFAAVERLMDYGMSSSHVLRN 1740
Db      1681  IDYDDITSVMKKEDDIYDEDENSPSPKQRTTRHYFAAVERLMDYGMSSSHVLRN 1740
Qy      1741  AOGSGVPQFKKVVFOEFTDGSFTQPLXRGELNEHLGLLPYTRAEVDNIMWTERQAS 1800
Db      1741  AOGSGVPQFKKVVFOEFTDGSFTQPLXRGELNEHLGLLPYTRAEVDNIMWTERQAS 1800
Qy      1801  PYSEYSSLIYEREDQOGAEPKRNKVPKNETKYFMKVOHHAAPTKEFDCKAAYESDY 1860
Db      1801  PYSEYSSLIYEREDQOGAEPKRNKVPKNETKYFMKVOHHAAPTKEFDCKAAYESDY 1860
Qy      1861  DLEKDVHSLGLPGLVCHNTNLNPAHQRYTVQEFALFTTIDETKSYFTENNERCRA 1920
Db      1861  DLEKDVHSLGLPGLVCHNTNLNPAHQRYTVQEFALFTTIDETKSYFTENNERCRA 1920
Qy      1921  PCNTQMEDPTFKENYFHAINGYIMDTLPGLVMAODQRIRWYLLSMGSNENIHSIHPSGH 1980
Db      1921  PCNTQMEDPTFKENYFHAINGYIMDTLPGLVMAODQRIRWYLLSMGSNENIHSIHPSGH 1980
Qy      1981  VFTVRKKKEEKMALVNLVPGVEFEVEMLPKAGIWRRECLIGEHLAGMSTLFLVYSNKC 2040
Db      1981  VFTVRKKKEEKMALVNLVPGVEFEVEMLPKAGIWRRECLIGEHLAGMSTLFLVYSNKC 2040
Qy      2041  QTPGMAHGHIRDFOTASGOYGOMAPRLARLHYSOSINAMSTKPEPMKIVDILAMIT 2100
Db      2041  QTPGMAHGHIRDFOTASGOYGOMAPRLARLHYSOSINAMSTKPEPMKIVDILAMIT 2100
Qy      2101  HGKTQGAQKQESSLIYSQFIIMSLSGKKMQRYSNGSTGLMVEFGVNDSSGIKHNIFN 2160
Db      2101  HGKTQGAQKQESSLIYSQFIIMSLSGKKMQRYSNGSTGLMVEFGVNDSSGIKHNIFN 2160
Qy      2161  PRIIARYIRLHPHYRISRTLMELMGDINSMPLEGESKAISDAQITSSYFTMFA 2220
Db      2161  PRIIARYIRLHPHYRISRTLMELMGDINSMPLEGESKAISDAQITSSYFTMFA 2220
Qy      2221  TWSPSKARHLQGRSNAMRPQVNNPKEMLYDQKTMKYTGVTTOGVASLLTSMYKEEL 2280
Db      2221  TWSPSKARHLQGRSNAMRPQVNNPKEMLYDQKTMKYTGVTTOGVASLLTSMYKEEL 2280
Qy      2281  ISSQDGHQWTLRFQNGKVKYFQGNDSFTPVVNSLDPLLTRYLRIHPQSWVHQIALRM 2340
Db      2281  ISSQDGHQWTLRFQNGKVKYFQGNDSFTPVVNSLDPLLTRYLRIHPQSWVHQIALRM 2340
Qy      2341  EVLGEAODLY 2351
Db      2341  EVLGEAODLY 2351

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FH      Key      Location/Qualifiers
FT      Peptide      1..19
FT      Protein      /note="signal peptide"
FT      Region      20..2351
FT      Modified-site 20..1667
FT      Region      /note="mature Factor VIII:C"
FT      Region      /note="heavy chain fragment"
FT      Region      /label= Phe, Glu, Pro
FT      Domain      1668..2350
FT      Domain      /note="light chain fragment"
FT      Domain      760..1667
FT      Domain      /note= "B domain"
PN      MO9703195-A1.
XX
XX      30-JAN-1997.
XX
XX      09-JUL-1996; 96MO-US11444.
XX
XX      11-JUL-1995; 95US-0001025.
XX
XX      (CHIR ) CHIRON CORP.
XX
XX      Cohen FE, Hung DT, Innis M;
XX      WPI; 1997-119050/11.
XX
XX      Factor VIII:C analog modified adjacent to a non-activating Arg
XX      residue - used in the treatment of haemophilias, by improvement of
XX      haemostasis
XX
XX      Claim 26; Page -: 90pp; English.
XX
XX      AAM11330-M1472 represent active Factor VIII:C analogues of the
XX      invention. These sequences were created by mutating the wild type Factor
XX      VIII:C coding sequence (see AAT51357) using mutagenic primers. The
XX      analogues comprise a native Factor VIII:C polypeptide modified at a site
XX      adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
XX      dipeptide is created. Factor VIII:C is a large glycoprotein that
XX      participates in the blood coagulation cascade that ultimately converts
XX      soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
XX      deficiency in Factor VIII:C is responsible for haemophilia A, which is an
XX      X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
XX      activated by plasma proteases, such as thrombin. During activation the
XX      mature polypeptide is cleaved to generate heavy and light chain fragments
XX      that are further cleaved. Complexes of two or more of the analogues,
XX      nucleic acids and vectors encoding them may be used alone or in
XX      conjunction with each other, for the prevention or treatment of active
XX      Factor VIII:C deficiency in a mammal. The analogues may be used as
XX      immunogens to raise antibodies, and in the treatment of haemophilias, by
XX      improvement of haemostasis. The analogues are resistant to proteolytic
XX      cleavage and display increased plasma half-life. They may be administered
XX      at lower dosages and by different modes of administration.
XX
XX      Sequence 2351 AA:
XX
XX      Query Match      100.0%; Score 12414; DB 18; Length 2351;
XX      Best Local Similarity 100.0%; Pred. No. 0;
XX      Matches 2350; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

```



QY	181	DLVKDANSGILGALVCRESLAKETQTHKFLFLPAVYDEKSMHSESTKNSLMODR	240
Db	181	VDLYKDNISGILGALVCRESLAKETQTHKFLFLPAVYDEKSMHSESTKNSLMODR	240
QY	241	AASRARAPKMHVYNGYVRSPLGLGCHKRSYVMVHIGMGTTPVHVSIFLEGTFLVYRH	300
Db	241	AASRARAPKMHVYNGYVRSPLGLGCHKRSYVMVHIGMGTTPVHVSIFLEGTFLVYRH	300
QY	301	ROASLEISPTFLTAOTLMDLGOFLFCHISHOHDMEMVYVVSCEPEROLPMKNE	360
Db	301	ROASLEISPTFLTAOTLMDLGOFLFCHISHOHDMEMVYVVSCEPEROLPMKNE	360
QY	361	EAEYDODDLDESMYVFFDDNSPSTQISRAVKKHKTWVHIAAEEEDMDYAPLVA	420
Db	361	EAEYDODDLDESMYVFFDDNSPSTQISRAVKKHKTWVHIAAEEEDMDYAPLVA	420
QY	421	PDDSYYSOYLLNGGQRIIGRKYYKVPMAVTEBTKTEALIOHSSGILGFLYGVGTL	480
Db	421	PDDSYYSOYLLNGGQRIIGRKYYKVPMAVTEBTKTEALIOHSSGILGFLYGVGTL	480
QY	481	LIFIKNOASFPYIYTHGIDVYRPLYSRRLPGVKYHLDPFLPGETIKMTVYEDCP	540
Db	481	LIFIKNOASFPYIYTHGIDVYRPLYSRRLPGVKYHLDPFLPGETIKMTVYEDCP	540
QY	541	TKSDPRCLTXYYSFVNNERDLASGLIGRPLITCYKESYDQAGNOIMSDKANNILTSVDE	600
Db	541	TKSDPRCLTXYYSFVNNERDLASGLIGRPLITCYKESYDQAGNOIMSDKANNILTSVDE	600
QY	601	NRSYUYLENIOFLRPLPAGVOLFEDPEFOASNIHMSINGYVDSIQLSVCHEAAWYILS	660
Db	601	NRSYUYLENIOFLRPLPAGVOLFEDPEFOASNIHMSINGYVDSIQLSVCHEAAWYILS	660
QY	661	IGAOITDLSYFSGTGFPHKVVYEDTLTPRPSGEVFMSENGMLIIGCHNSPFRNG	720
Db	661	IGAOITDLSYFSGTGFPHKVVYEDTLTPRPSGEVFMSENGMLIIGCHNSPFRNG	720
QY	721	MFALLKYSQCDKATGYEDSYEDISAYLKSNNALIPRSTSONSRHSTROKOFNATTI	780
Db	721	MFALLKYSQCDKATGYEDSYEDISAYLKSNNALIPRSTSONSRHSTROKOFNATTI	780
QY	781	PENDIEKTDQWFAHRTPMKTIOWYSSDLDMLKROSPRPHGLSLSDLOEKAYETSDPS	840
Db	781	PENDIEKTDQWFAHRTPMKTIOWYSSDLDMLKROSPRPHGLSLSDLOEKAYETSDPS	840
QY	841	PGAIDSNNSLSEKTHRRDOLHNSGDVYFPESGLQILINELKIGTATTELKIDFVYST	900
Db	841	PGAIDSNNSLSEKTHRRDOLHNSGDVYFPESGLQILINELKIGTATTELKIDFVYST	900
QY	901	SNNLITSTIPBDNLAAAGTQNTSGLPBPMPHYHYSOQDITLTKGKSSPLTSGSPSLSE	960
Db	901	SNNLITSTIPBDNLAAAGTQNTSGLPBPMPHYHYSOQDITLTKGKSSPLTSGSPSLSE	960
QY	961	NNSKLLIESGLMNSOESSWGNKNSVSTSGFLFKGRKHAHPALLTKDNALFKVYSILKTN	1020
Db	961	NNSKLLIESGLMNSOESSWGNKNSVSTSGFLFKGRKHAHPALLTKDNALFKVYSILKTN	1020
QY	1021	KTSNNSATNKTHTIDGSPSLIENSPSWOMILSDIEFEKATYPLIHRMLMDNATATL	1080
Db	1021	KTSNNSATNKTHTIDGSPSLIENSPSWOMILSDIEFEKATYPLIHRMLMDNATATL	1080
QY	1081	NHMSNKTSSKNMEMVOQKEGPIPPAQNPDMSFFKMLFIPRESARVIOETHKNSLNG	1140
Db	1081	NHMSNKTSSKNMEMVOQKEGPIPPAQNPDMSFFKMLFIPRESARVIOETHKNSLNG	1140
QY	1141	QGPBPOLVLSLGEKSVBQNFLESKKNVYVGGETDYGLKAMPSPSRNLTFLNND	1200
Db	1141	QGPBPOLVLSLGEKSVBQNFLESKKNVYVGGETDYGLKAMPSPSRNLTFLNND	1200
QY	1201	LHNNNTNOEKTOEIEITEKFTLQIENVVLPOLHTYGTGNKMNKULFLSTRONVBSYD	1260
Db	1201	LHNNNTNOEKTOEIEITEKFTLQIENVVLPOLHTYGTGNKMNKULFLSTRONVBSYD	1260
QY	1261	GAVPVLODERSLNSSTNKTAKHTAHFSKSGEENLEBIGNDQTOIYEKACTRISPT	1320

Db	1261	GATAPVLODPSRLNDSJTRTKKHTAHFSSKKGBEENJDELGNOJTOYEXACTRILSPNT	1320
Qy	1321	SCQNFYQNSKRALQOFRLPLEELEEKRIYDQSTQNSKNNKHLTPSTLQIDYNEKE	1380
Db	1321	SOQNFYQNSKRALQOFRLPLEELEEKRIYDQSTQNSKNNKHLTPSTLQIDYNEKE	1380
Qy	1381	KGATIOSPLSDCLTRSHSIPQANRSPRLIAKVSFSPSIRPYLTRVLFQDNSSHLPAA5Y	1440
Db	1381	KGATIOSPLSDCLTRSHSIPQANRSPRLIAKVSFSPSIRPYLTRVLFQDNSSHLPAA5Y	1440
Qy	1441	RKKSQGVQESSHFLQAKKNNLSLAITLBMGDQRENGSLGTSATNSYKKEVENTYLP	1500
Db	1441	RKKSQGVQESSHFLQAKKNNLSLAITLBMGDQRENGSLGTSATNSYKKEVENTYLP	1500
Qy	1501	KPDLPTKSGVELLPRVHYHOKDLEPPTNSPGHLDVYSGLSLOQTEBAILKMNANRP	1560
Db	1501	KPDLPTKSGVELLPRVHYHOKDLEPPTNSPGHLDVYSGLSLOQTEBAILKMNANRP	1560
Qy	1561	KNVPLLVNATESSAKTPSKLDPRLAMDNHGTQIPEKMSQEKSPKTAFFKKOTJL5L	1620
Db	1561	KNVPLLVNATESSAKTPSKLDPRLAMDNHGTQIPEKMSQEKSPKTAFFKKOTJL5L	1620
Qy	1621	NACESNHAIAINEGONKREIEVYMAQGTERTLCSQNPVLKRHRQREITRTLQSDOE	1680
Db	1621	NACESNHAIAINEGONKREIEVYMAQGTERTLCSQNPVLKRHRQREITRTLQSDOE	1680
Qy	1681	IDYODTISVEMKKEPDYIDEDENQSRSRQKTRHRYEIAAVERLAMYQSSSPHYLNR	1740
Db	1681	IDYODTISVEMKKEPDYIDEDENQSRSRQKTRHRYEIAAVERLAMYQSSSPHYLNR	1740
Qy	1741	AQSGSVQPFKKVYVOEFGDGSFTQPLRGELNHLGILLGPYIIRAVEDNIMYTFRNOASR	1800
Db	1741	AQSGSVQPFKKVYVOEFGDGSFTQPLRGELNHLGILLGPYIIRAVEDNIMYTFRNOASR	1800
Qy	1801	PYSEYSSLISEEDQOQAEPRKAPYVPRNETKITRYKQVQHNMAATKREBPCKAKAYFSDY	1860
Db	1801	PYSEYSSLISEEDQOQAEPRKAPYVPRNETKITRYKQVQHNMAATKREBPCKAKAYFSDY	1860
Qy	1861	DLEKDVHSGILGFLVCHNHTLPAHGRQVYVQEFALFTTJFDETKSMYTEMMERNCRA	1920
Db	1861	DLEKDVHSGILGFLVCHNHTLPAHGRQVYVQEFALFTTJFDETKSMYTEMMERNCRA	1920
Qy	1921	PCNIONMDPFEKKNYFENHANGYIMDLPECLVAAQORAIRMYLLSMQSNENHISHFSGH	1980
Db	1921	PCNIONMDPFEKKNYFENHANGYIMDLPECLVAAQORAIRMYLLSMQSNENHISHFSGH	1980
Qy	1981	VPTYRKKEEKEMALYLVXGVFEYVEMLPKAGIMVBECLGELHLAGNSTLPIYVSKNC	2040
Db	1981	VPTYRKKEEKEMALYLVXGVFEYVEMLPKAGIMVBECLGELHLAGNSTLPIYVSKNC	2040
Qy	2041	QTPYLGMA5GHIRFOJTASGOYQOMAPKLARLH5GSIJNANSTSEPP5ATKVDLAPMTI	2100
Db	2041	QTPYLGMA5GHIRFOJTASGOYQOMAPKLARLH5GSIJNANSTSEPP5ATKVDLAPMTI	2100
Qy	2101	HQIKTQAGARQFSSLYISOFITIMYSLDGKKWQTYRGNSTGTLMVFGSNDSSGIRKHNIFN	2160
Db	2101	HQIKTQAGARQFSSLYISOFITIMYSLDGKKWQTYRGNSTGTLMVFGSNDSSGIRKHNIFN	2160
Qy	2161	PIIARIYIRLHPHYSIR5TILAMELMQCDLNSC5MPLGME5KASISDAQITASS5YFNMEA	2220
Db	2161	PIIARIYIRLHPHYSIR5TILAMELMQCDLNSC5MPLGME5KASISDAQITASS5YFNMEA	2220
Qy	2221	TW5PSKARLHLQORSNAMPPOVNNPKEMLOVDQKPMKYQVGTYYQGVKSLT5MYKEFL	2280
Db	2221	TW5PSKARLHLQORSNAMPPOVNNPKEMLOVDQKPMKYQVGTYYQGVKSLT5MYKEFL	2280
Qy	2281	ISS5QDGHQWTFEPQNGKKYVFOGNDQ5FPVNVNSLDPLLTRILRLIHPQ5VYHQJALBM	2340
Db	2281	ISS5QDGHQWTFEPQNGKKYVFOGNDQ5FPVNVNSLDPLLTRILRLIHPQ5VYHQJALBM	2340
Qy	2341	EVLGCEAQDLY 2351	

Db 2341 EVLACEA0DLX 2351

RESULT 8  
AAW11343  
ID AAW11343 standard; Protein; 2351 AA.  
AC AAW11343;  
XX  
DT 17-NOV-1997 (first entry)  
XX  
DE Active Factor VIII:C analogue S224X.  
XX  
KW Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;  
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KW plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;  
KM proteolytic cleavage.  
XX  
OS Homo sapiens.  
XX Synthetic.  
XX  
FH Key Location/Qualifiers  
FT Peptide 1..19  
FT /note= "signal peptide"  
FT Protein 20..2351  
FT /note= "mature Factor VIII:C"  
FT Region 20..1667  
FT /note= "heavy chain fragment"  
FT Modified-site 243  
FT /label= "Phe, Glu, Pro  
FT Region 1668..2350  
FT /note= "light chain fragment"  
FT Domain 760..1667  
FT /note= "B domain"  
XX  
PN WO9703195-A1.  
XX  
PD 30-JAN-1997.  
XX  
PF 09-JUL-1996; 96MO-US11444.  
XX  
PR 11-JUL-1995; 95US-0001025.  
XX  
PA (CHIR ) CHIRON CORP.  
XX  
PI Cohen FE, Hung DT, Innis M;  
XX WPI; 1997-119050/11.  
DR  
XX  
PT Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophiliacs, by improvement of  
PT haemostasis  
XX  
PS Claim 10; Page -: 90pp; English.  
XX  
CC AAW11330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophiliacs, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic

CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.

XX Sequence 2351 AA:

Query Match 100.0%; Score 12414; DB 18; Length 2351;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2350; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 1 MOTEISCFELLCFESATRRRYLGAVALSDMDQSDIGELPVDARPPRPKSFPPN 60  
DB 1 MOTEISCFELLCFESATRRRYLGAVALSDMDQSDIGELPVDARPPRPKSFPPN 60  
QY 61 TSVYKKTLEFETDHLFNIAKPPPMGLGFTIOAEVYDTVTYTLKNASHPVSLAV 120  
DB 61 TSVYKKTLEFETDHLFNIAKPPPMGLGFTIOAEVYDTVTYTLKNASHPVSLAV 120  
QY 121 GVSVMKASGAEYDQTSQREKEDDKVFPGSHYVMQVLKENGPMASDPLCLTYSYLSH 180  
DB 121 GVSVMKASGAEYDQTSQREKEDDKVFPGSHYVMQVLKENGPMASDPLCLTYSYLSH 180  
QY 181 VDLVKDLSGLGALLVREGSLAKKETQTLKFTLLRVNVDKSHSFTKSLMODD 240  
DB 181 VDLVKDLSGLGALLVREGSLAKKETQTLKFTLLRVNVDKSHSFTKSLMODD 240  
QY 241 AASARAMPKMTVNGYVNRSLPGLIGCHRSKYVMHYIGMTPPEVHSIFLEGHTFLVRNH 300  
DB 241 AASARAMPKMTVNGYVNRSLPGLIGCHRSKYVMHYIGMTPPEVHSIFLEGHTFLVRNH 300  
QY 301 ROSLSIESPTFLTQTLMDLGOFLFCHISSHODGMEAVYVDSCEPEPLRKNNE 360  
DB 301 ROSLSIESPTFLTQTLMDLGOFLFCHISSHODGMEAVYVDSCEPEPLRKNNE 360  
QY 361 EABDYDDLTDSEMDVYFRDDNSPSTQIRSYAKKHRTVWYHIAAEEEDWYAPVLA 420  
DB 361 EABDYDDLTDSEMDVYFRDDNSPSTQIRSYAKKHRTVWYHIAAEEEDWYAPVLA 420  
QY 421 PDDRSYKSOYLNNGFORIGRKYKRVPMATDETETKRAIOHESGILGLVGEVDTL 480  
DB 421 PDDRSYKSOYLNNGFORIGRKYKRVPMATDETETKRAIOHESGILGLVGEVDTL 480  
QY 481 LIIFKXNASPYNIYPHGITVPRFLYSRRIPKQVKHLDGFLFGEIFKKKMWYVEDP 540  
DB 481 LIIFKXNASPYNIYPHGITVPRFLYSRRIPKQVKHLDGFLFGEIFKKKMWYVEDP 540  
QY 541 TKSDPRCLRTYSSFVNMRDLASGLIGLICYKESVDQKNOIMSDKKNVLSVEDE 600  
DB 541 TKSDPRCLRTYSSFVNMRDLASGLIGLICYKESVDQKNOIMSDKKNVLSVEDE 600  
QY 601 NRSWYLTENIOREFLNPAGVOLDPEFOASINMHSINGVYDLSQLSVCLHEVAYWYILS 660  
DB 601 NRSWYLTENIOREFLNPAGVOLDPEFOASINMHSINGVYDLSQLSVCLHEVAYWYILS 660  
QY 661 IGAOTDFLSVFSFGYTFPKKMYVEDTLTLPFSGEIVMSNENGLMILCHNSDPRNNG 720  
DB 661 IGAOTDFLSVFSFGYTFPKKMYVEDTLTLPFSGEIVMSNENGLMILCHNSDPRNNG 720  
QY 721 MTALLKVSQDNKTDYEDSYEDISAVYLSKKNALIEPSSONSRRPSTRQOFNATTI 780  
DB 721 MTALLKVSQDNKTDYEDSYEDISAVYLSKKNALIEPSSONSRRPSTRQOFNATTI 780  
QY 781 PENDIEKTPWFARHTPMPKIQONVSSDILLMLRQSPPHGLSISDQEAKYTFSDPS 840  
DB 781 PENDIEKTPWFARHTPMPKIQONVSSDILLMLRQSPPHGLSISDQEAKYTFSDPS 840  
QY 841 PGALDSNLSSEMTFRROLHSDMWTFPESQDLRLNEKLGTTAATTELKIDFVYST 900  
DB 841 PGALDSNLSSEMTFRROLHSDMWTFPESQDLRLNEKLGTTAATTELKIDFVYST 900  
QY 901 SNNLSTIRSDMLAAGTDMTSSLCPPSMVHYDSOLDLTLTGKSSPLTESGGSLSEE 960  
DB 901 SNNLSTIRSDMLAAGTDMTSSLCPPSMVHYDSOLDLTLTGKSSPLTESGGSLSEE 960

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OY 961 NNDKLLSGLMSQESSMGKNVSTESGRLFKKRAHGRALLTKDNALFYKYSISLKTN 1020
    |||
DB 961 NNDKLLSGLMSQESSMGKNVSTESGRLFKKRAHGRALLTKDNALFYKYSISLKTN 1020
OY 1021 KTSNNSATNRKTHIDGSPSLLIENSPPVQNTLESDETEFFKVTPLJHDMRLMDKNAZALRL 1080
    |||
DB 1021 KTSNNSATNRKTHIDGSPSLLIENSPPVQNTLESDETEFFKVTPLJHDMRLMDKNAZALRL 1080
OY 1081 NMSNKTTSKKNMENVQOKKEGPIPPDAQNDPMDFFKMLFLPESARMIORTHGKNSLNG 1140
    |||
DB 1081 NMSNKTTSKKNMENVQOKKEGPIPPDAQNDPMDFFKMLFLPESARMIORTHGKNSLNG 1140
OY 1141 OGPSPKOLVSLGPEKSYEGONFLSRKNVYVKGEEPTKVDGLKEMVFPSSRLFLTNLDN 1200
    |||
DB 1141 OGPSPKOLVSLGPEKSYEGONFLSRKNVYVKGEEPTKVDGLKEMVFPSSRLFLTNLDN 1200
OY 1201 LHENTHNOEKKIOEIEIEKKEFTLIOENVLPQIHFTVTGTAKNFKNLFLSTROVNEGSYD 1260
    |||
DB 1201 LHENTHNOEKKIOEIEIEKKEFTLIOENVLPQIHFTVTGTAKNFKNLFLSTROVNEGSYD 1260
OY 1261 GAYAPVLQDFRSLNDSTNRTKKHTAFSKGGEENLEGLNQTKQIVEKYACTRISBNT 1320
    |||
DB 1261 GAYAPVLQDFRSLNDSTNRTKKHTAFSKGGEENLEGLNQTKQIVEKYACTRISBNT 1320
OY 1321 SOONFVTORSKRALKOPRLDEETLEKRIIVYDPTSONSKNMKHLTPSTLQIDYNEKE 1380
    |||
DB 1321 SOONFVTORSKRALKOPRLDEETLEKRIIVYDPTSONSKNMKHLTPSTLQIDYNEKE 1380
OY 1381 KGAITQSPSLDCILTRSHSIPQANRSPPLIAVSSFPSIRPIYLTVRLVQDNSSHLPAASY 1440
    |||
DB 1381 KGAITQSPSLDCILTRSHSIPQANRSPPLIAVSSFPSIRPIYLTVRLVQDNSSHLPAASY 1440
OY 1441 RKKDSGVOESSHFLQGAKKNNLSLAILLEMTGQORVNGSLGTSANSTVYKKEVNTVLP 1500
    |||
DB 1441 RKKDSGVOESSHFLQGAKKNNLSLAILLEMTGQORVNGSLGTSANSTVYKKEVNTVLP 1500
OY 1501 KPDLPTSGKVELLPKYHIYOKDLPTETSSNGSGHLDIVESGLQGTGALAKWMEANRP 1560
    |||
DB 1501 KPDLPTSGKVELLPKYHIYOKDLPTETSSNGSGHLDIVESGLQGTGALAKWMEANRP 1560
OY 1561 GAYPFLRAVATESAKTYSKLLDPLANDNHGTOIPKEEMKSOEKSPERTAKFKKDTJISL 1620
    |||
DB 1561 GAYPFLRAVATESAKTYSKLLDPLANDNHGTOIPKEEMKSOEKSPERTAKFKKDTJISL 1620
OY 1621 NCESNHAIAAINEGQNKPEIEVYNAKOGKTERLCSONPVLRKHOREITRTTLOSDEE 1680
    |||
DB 1621 NCESNHAIAAINEGQNKPEIEVYNAKOGKTERLCSONPVLRKHOREITRTTLOSDEE 1680
OY 1681 IDYDPTISVEAKKEDFDIYDEENOSPSPFOKTRHYFIAVBRMDYGMSSSPHVLBNR 1740
    |||
DB 1681 IDYDPTISVEAKKEDFDIYDEENOSPSPFOKTRHYFIAVBRMDYGMSSSPHVLBNR 1740
OY 1741 AOSGSVPQFKVVOEFTDGSFTQPLYKGLANHLGLGPLYIAEVEDNIMVTFPNOASR 1800
    |||
DB 1741 AOSGSVPQFKVVOEFTDGSFTQPLYKGLANHLGLGPLYIAEVEDNIMVTFPNOASR 1800
OY 1801 PYSFYSLSIYEEDOROGAEPKRNFKVNETKYTFVKVOHHMAPTKDEFDCKAMAYFSDV 1860
    |||
DB 1801 PYSFYSLSIYEEDOROGAEPKRNFKVNETKYTFVKVOHHMAPTKDEFDCKAMAYFSDV 1860
OY 1861 DLEKDVHSGILGPLLYCHTNTLNPAGROVYVOEALFPTIPDETCSWTFETNMERNORA 1920
    |||
DB 1861 DLEKDVHSGILGPLLYCHTNTLNPAGROVYVOEALFPTIPDETCSWTFETNMERNORA 1920
OY 1921 PCNIQMEDPTREKYNRRHAINGTIMDTLGLVMAQDORIMYTLISGNSMENHSHIFSGH 1980
    |||
DB 1921 PCNIQMEDPTREKYNRRHAINGTIMDTLGLVMAQDORIMYTLISGNSMENHSHIFSGH 1980
OY 1981 VFTVRKKEBYKMALYNLPGVFETVEMLPKSKAGIMRWECCLIGELHLAGSTLFLVYSNKC 2040
    |||
DB 1981 VFTVRKKEBYKMALYNLPGVFETVEMLPKSKAGIMRWECCLIGELHLAGSTLFLVYSNKC 2040
OY 2041 QPPLGASGHI RDOFQITASQYQGMAMPKLARLHLSGSIINAMSTKKEPFSNIKTVDLAPRIL 2100

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DB 2041 QPPLGASGHI RDOFQITASQYQGMAMPKLARLHLSGSIINAMSTKKEPFSNIKTVDLAPRIL 2100
    |||
OY 2101 HGIKTGAROKFSSSLYSOFIIMVSLDCKMOTYRKGNSTGTLMEVFGVNDSSGIKHNIN 2160
    |||
DB 2101 HGIKTGAROKFSSSLYSOFIIMVSLDCKMOTYRKGNSTGTLMEVFGVNDSSGIKHNIN 2160
OY 2161 PPIIARIYRIHPHYISIRSTLMELMGCDLNSCSMPLGMEKSAISDAQITASSYFTNMFA 2220
    |||
DB 2161 PPIIARIYRIHPHYISIRSTLMELMGCDLNSCSMPLGMEKSAISDAQITASSYFTNMFA 2220
OY 2221 TWSPSKARLILQGRSNAMRPVNNPKEMLDVDFOKMTKYTVTQGVKSILTSMYKEFL 2280
    |||
DB 2221 TWSPSKARLILQGRSNAMRPVNNPKEMLDVDFOKMTKYTVTQGVKSILTSMYKEFL 2280
OY 2281 ISSSODGHQWTLFFONGKVKVFOGNQDSFTPPVNSLDPLLTRYLRIHPOSWHQIALRM 2340
    |||
DB 2281 ISSSODGHQWTLFFONGKVKVFOGNQDSFTPPVNSLDPLLTRYLRIHPOSWHQIALRM 2340
OY 2341 EYLGCEAODLY 2351
    |||
DB 2341 EYLGCEAODLY 2351
    |||

RESULT 9
AA011461
ID AA011461 standard; Protein; 2351 AA.
XX
AC AA011461;
XX
DT 20-NOV-1997 (first entry)
XX
DE Active Factor VIII:C analogue V1717X.
XX
KW Factor VIII:C analogue; glycoprotein; blood coagulation cascade;
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW proteolytic cleavage.
XX
OS Homo sapiens.
XX
OS Synthetic.
XX
FH key
FT 1..19 Location/Qualifiers
FT /note= "signal peptide"
FT 20..2351
FT /note= "mature Factor VIII:C"
FT Region
FT 20..1667
FT /note= "heavy chain fragment"
FT 1668..2350
FT /note= "light chain fragment"
FT Domain
FT 760..1667
FT /note= "b domain"
FT Modified-site
FT 1736
FT /label= Phe, Glu, Pro

w09703195-A1.
30-JAN-1997.
09-JUL-1996; 96MO-US11444.
11-JUL-1995; 95US-0001025.
(CHIR ) CHIRON CORP.
Cohen FE, Hung DT, Innis M;
WPI: 1997-119050/11.
Factor VIII:C analog modified adjacent to a non-activating Arg
residue - used in the treatment of haemophiliacs, by improvement of
hemostasis

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XX Claim 36; Page -: 90pp; English.

XX  
CC AAM1330-W1472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAF51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophiliacs, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.

XX Sequence 2351 AA:

Query Match 100.0%; Score 12413; DB 18; Length 2351;

Best local Similarity 100.0%; Pred. No. 0;

Matches 2350; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 1 MOELSTCFCLLRCSATRRYYLGAVELSMYQSDLGELPDARPPRRVRSPPN 60  
DB 1 MOELSTCFCLLRCSATRRYYLGAVELSMYQSDLGELPDARPPRRVRSPPN 60  
QY 61 TSVYKRTLFVEETDHLFNIAKRPMMGLGPTIOAEVYDVYITLKNMASHPVSLAAV 120  
DB 61 TSVYKRTLFVEETDHLFNIAKRPMMGLGPTIOAEVYDVYITLKNMASHPVSLAAV 120  
QY 121 GVSYWKASGEAEYDDOTSOREKEDKVPGGSHYVQVYKENGMAADPCLTYSTLSH 180  
DB 121 GVSYWKASGEAEYDDOTSOREKEDKVPGGSHYVQVYKENGMAADPCLTYSTLSH 180  
QY 181 VDLKYNLSGLIGALLYCREGSLAKEKQTLAKTLLFAVDEGKSMHSEKNSLMDRD 240  
DB 181 VDLKYNLSGLIGALLYCREGSLAKEKQTLAKTLLFAVDEGKSMHSEKNSLMDRD 240  
QY 241 AASARAPKMHYNGVYNSLPGLIGCHRSKVYWHYIGMGTPEVHSLFEGHTFLVRNH 300  
DB 241 AASARAPKMHYNGVYNSLPGLIGCHRSKVYWHYIGMGTPEVHSLFEGHTFLVRNH 300  
QY 301 ROASLEISPTITLTAOTLLMDLGGPLFCCHSHSHOHGMAEYKVDSCPEPOLRMKNNE 360  
DB 301 ROASLEISPTITLTAOTLLMDLGGPLFCCHSHSHOHGMAEYKVDSCPEPOLRMKNNE 360  
QY 361 PAEDYDDDLDSMDVYRFDNNSPQTQTSVAKKHPTWYHYYIAEEDMDVAPLVYA 420  
DB 361 PAEDYDDDLDSMDVYRFDNNSPQTQTSVAKKHPTWYHYYIAEEDMDVAPLVYA 420  
QY 421 PDDRSYSQYLLNNGPQIRKKYKVFMAYYTDEFKTRREALIHESGILGPLLYGEVDTL 480  
DB 421 PDDRSYSQYLLNNGPQIRKKYKVFMAYYTDEFKTRREALIHESGILGPLLYGEVDTL 480  
QY 481 LIIFKNOASRPYNIYHGITDVRPLYSRRLPKGKHLKDPPLPGIFRYKMYATVEDGP 540  
DB 481 LIIFKNOASRPYNIYHGITDVRPLYSRRLPKGKHLKDPPLPGIFRYKMYATVEDGP 540  
QY 541 TKSDEPCLTRYYSFVNMERDIASGLIGPLLYCYKESVDORGNQMSDKRVNLLFSEVDE 600  
DB 541 TKSDEPCLTRYYSFVNMERDIASGLIGPLLYCYKESVDORGNQMSDKRVNLLFSEVDE 600  
QY 601 NRSWYLTENIORFLPPAGVQLEDEFOASNMHMSINGYFQSLQSLCYLEVAWYITLS 660  
DB 601 NRSWYLTENIORFLPPAGVQLEDEFOASNMHMSINGYFQSLQSLCYLEVAWYITLS 660

QY 661 IGAOTDELVSFESGYTFKHKMYEDTLTLPEFSGETVEKSMENPGMLTLCGHSNDRNNG 720  
DB 661 IGAOTDELVSFESGYTFKHKMYEDTLTLPEFSGETVEKSMENPGMLTLCGHSNDRNNG 720  
QY 721 MTALKKVSQDKMTGDIYEDSYEDISALYLSKNNALPEPFSQNSRRPSTROKOPNATPI 780  
DB 721 MTALKKVSQDKMTGDIYEDSYEDISALYLSKNNALPEPFSQNSRRPSTROKOPNATPI 780  
QY 781 PENDIEKDFWFAHRTPMFKIQWYSSDILLMLROSPPHGISLSDLOEAKYEFSDDS 840  
DB 781 PENDIEKDFWFAHRTPMFKIQWYSSDILLMLROSPPHGISLSDLOEAKYEFSDDS 840  
QY 841 PGALDSNNSISEKTHPRPOLNHSQDMVFTPESGLORLNEKIGTTAATELKIDFVYSST 900  
DB 841 PGALDSNNSISEKTHPRPOLNHSQDMVFTPESGLORLNEKIGTTAATELKIDFVYSST 900  
QY 901 SNNLISTPBDNLAAGTQNTSILGPPMPYHVSQDPTTLGKSSPITSSGGPLSLSE 960  
DB 901 SNNLISTPBDNLAAGTQNTSILGPPMPYHVSQDPTTLGKSSPITSSGGPLSLSE 960  
QY 961 MDSKLLSEGLMNSQESSGKNVSTESGRLEFKGRABGALLTKDNALRKVSLSLKTN 1020  
DB 961 MDSKLLSEGLMNSQESSGKNVSTESGRLEFKGRABGALLTKDNALRKVSLSLKTN 1020  
QY 1021 KTSNNSATNFKTHIDPSSLTLENSPVMQNTLESDFEKKVYPLTIHDMMLMDKNATATRL 1080  
DB 1021 KTSNNSATNFKTHIDPSSLTLENSPVMQNTLESDFEKKVYPLTIHDMMLMDKNATATRL 1080  
QY 1081 NHMSNKTSSKNMEOOKKEGPIIPPAQONPDMSPFKMLFLPESARMTIOPHKNLSNNG 1140  
DB 1081 NHMSNKTSSKNMEOOKKEGPIIPPAQONPDMSPFKMLFLPESARMTIOPHKNLSNNG 1140  
QY 1141 QGSPKOLVSLGPEKSVBQONFLSEKKNVVYGERTKQVGLAKEMVPPSSRNIFLTINDN 1200  
DB 1141 QGSPKOLVSLGPEKSVBQONFLSEKKNVVYGERTKQVGLAKEMVPPSSRNIFLTINDN 1200  
QY 1201 LAENNTNHOEKKIOEIEIEKETLLIOENVVLPQIHVTGKFNKMLFLSTRONVGSYD 1260  
DB 1201 LAENNTNHOEKKIOEIEIEKETLLIOENVVLPQIHVTGKFNKMLFLSTRONVGSYD 1260  
QY 1261 GAVAPVQDPRSTNOSTNTKTHAHSKKEEENLEGIQNTQIYKVACTRTISPT 1320  
DB 1261 GAVAPVQDPRSTNOSTNTKTHAHSKKEEENLEGIQNTQIYKVACTRTISPT 1320  
QY 1321 SQONFVTOQRKALKOFLPLEETELEKRIIVDSTQNSKMKHLPTSTLTQIDYNEKE 1380  
DB 1321 SQONFVTOQRKALKOFLPLEETELEKRIIVDSTQNSKMKHLPTSTLTQIDYNEKE 1380  
QY 1381 KGATTOGSLDCLTRSHSIPQANSPLPIAKVSPSPSIRPIYTLRVLEFQDNSSHLPAASY 1440  
DB 1381 KGATTOGSLDCLTRSHSIPQANSPLPIAKVSPSPSIRPIYTLRVLEFQDNSSHLPAASY 1440  
QY 1441 RKKDSGVQESSHFLQAKKNNLSALITLMTQDQREVSGLSTSTNSVYKYKVENTVLP 1500  
DB 1441 RKKDSGVQESSHFLQAKKNNLSALITLMTQDQREVSGLSTSTNSVYKYKVENTVLP 1500  
QY 1501 KPDLPTKSGVVELLPKVHITYOKDLPEPTESNGSPGLDLYVESLLQGTGEGAKMNEANRP 1560  
DB 1501 KPDLPTKSGVVELLPKVHITYOKDLPEPTESNGSPGLDLYVESLLQGTGEGAKMNEANRP 1560  
QY 1561 GKVPFLVATRESSAKIPSKLDPALAMNHNQGTQIPKEEMKSOEKSPEKTAFAKKDITLSL 1620  
DB 1561 GKVPFLVATRESSAKIPSKLDPALAMNHNQGTQIPKEEMKSOEKSPEKTAFAKKDITLSL 1620  
QY 1621 NACSSNNAIAINEGONKELEYMAOQTEBELCQONPVYLRHOREITRTYLIQSDQEE 1680  
DB 1621 NACSSNNAIAINEGONKELEYMAOQTEBELCQONPVYLRHOREITRTYLIQSDQEE 1680  
QY 1681 IDYDITISVEMKKEDEDIYDEDENSPSPQKTRHYFLAAVERLMDYGMSSPHVLRNR 1740  
DB 1681 IDYDITISVEMKKEDEDIYDEDENSPSPQKTRHYFLAAVERLMDYGMSSPHVLRNR 1740

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QY 1741 AAGSGVPOFKKVFQOEFTDGSFTQPYRGELNENHGLIGLSPYIRAEVDNIMTFERNQASR 1800
DB 1741 AAGSGVPOFKKVFQOEFTDGSFTQPYRGELNENHGLIGLSPYIRAEVDNIMTFERNQASR 1800
QY 1801 PYSFTSSLSISTEEDROGAEPKRNPKVNETKTFYFWKVQHMAPTKDEFDCKAMAYFSDV 1860
DB 1801 PYSFTSSLSISTEEDROGAEPKRNPKVNETKTFYFWKVQHMAPTKDEFDCKAMAYFSDV 1860
QY 1861 DLEKDVHSGLLGPLLVCHTNTLPNPAHROVYVQOEALFEFTFDETSKSWTFENMERNCRA 1920
DB 1861 DLEKDVHSGLLGPLLVCHTNTLPNPAHROVYVQOEALFEFTFDETSKSWTFENMERNCRA 1920
QY 1921 PCNIOMEDPTREKYNRRHAINGTIMPTLPGIYMAODQIRWYLLISGNSMENHSHFSGH 1980
DB 1921 PCNIOMEDPTREKYNRRHAINGTIMPTLPGIYMAODQIRWYLLISGNSMENHSHFSGH 1980
QY 1981 VFTVRKKEEYKALYNLYPGVFETVEMLPKAGIWRVECLIGEHLAGNSTLFLVYSNKC 2040
DB 1981 VFTVRKKEEYKALYNLYPGVFETVEMLPKAGIWRVECLIGEHLAGNSTLFLVYSNKC 2040
QY 2041 QPPLGMASGHTRDFOITASGOYCOMAPKILARLHYSGSINAMSTKEPSPWIKYDLLAPMI 2100
DB 2041 QPPLGMASGHTRDFOITASGOYCOMAPKILARLHYSGSINAMSTKEPSPWIKYDLLAPMI 2100
QY 2101 HGKIQGAKRKFSSTYSISOFITMSIDGKKNOTYRGNSTGTLMWFGSNDDSGIKHNIFN 2160
DB 2101 HGKIQGAKRKFSSTYSISOFITMSIDGKKNOTYRGNSTGTLMWFGSNDDSGIKHNIFN 2160
QY 2161 PPIIARYIRLPHFHSYIRSTLRMELMGCDLNSCMPLOGMESKASIDAOITASSYFTNFA 2220
DB 2161 PPIIARYIRLPHFHSYIRSTLRMELMGCDLNSCMPLOGMESKASIDAOITASSYFTNFA 2220
QY 2221 TMSPSKARLHLOGRNSNAPROVNNPKEMLOVFOKTMKVTVTGTQGVKSLTSMYVKEL 2280
DB 2221 TMSPSKARLHLOGRNSNAPROVNNPKEMLOVFOKTMKVTVTGTQGVKSLTSMYVKEL 2280
QY 2281 ISSSDGQHMTLFRONKRYVFGQNDSTFPVNSLDPLLTRILRIHQSWHQAIALRM 2340
DB 2281 ISSSDGQHMTLFRONKRYVFGQNDSTFPVNSLDPLLTRILRIHQSWHQAIALRM 2340
QY 2341 EYLGCENADLY 2351
DB 2341 EYLGCENADLY 2351

RESULT 10
AAM11445
ID AAM11445 standard; Protein: 2351 AA.
XX
AC AAM11445;
XX
DT 20-NOV-1997 (first entry)
XX
DE Active Factor VIII:C analogue L1643X.
XX
KM Factor VIII:C analogue; glycoprotein; blood coagulation cascade;
KM fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KM plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;
KM proteolytic cleavage.
XX
OS Homo sapiens.
OS Synthetic.
XX
FH Key 1.19 Location/Qualifiers
FH Peptide /note= "signal peptide"
FH FT 20..2351
FH FT Protein /note= "mature Factor VIII:C"
FH FT Region 20..1667
FH FT /note= "heavy chain fragment"
FH FT Modified-site 1662
FH FT /label= Phe, Glu, Pro
FH FT Region 1668..2350
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FT /note= "light chain fragment"
FT 760..1667
FT /note= "B domain"
DB MO9703195-A1.
DB 30-JAN-1997.
DB 09-JUL-1996; 96MO-US11444.
DB 11-JUL-1995; 95US-0001025.
DB (CHIR ) CHIRON CORP.
DB Cohen FE, Hung DT, Innis M;
DB WPI: 1997-119050/11.
DB
DB Factor VIII:C analog modified adjacent to a non-activating Arg
DB residue - used in the treatment of haemophilias, by improvement of
DB haemostasis
DB
DB Claim 32; Page -, 90pp; English.
DB
DB AAM11330-W11472 represent active Factor VIII:C analogues of the
DB invention. These sequences were created by mutating the wild type Factor
DB VIII:C coding sequence (see AAT51357) using mutagenic primers. The
DB analogues comprise a native Factor VIII:C polypeptide modified at a site
DB adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
DB dipeptide is created. Factor VIII:C is a large glycoprotein that
DB participates in the blood coagulation cascade that ultimately converts
DB soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
DB deficiency in Factor VIII:C is responsible for haemophilia A, which is an
DB X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
DB activated by plasma proteases, such as thrombin. During activation the
DB mature polypeptide is cleaved to generate heavy and light chain fragments
DB that are further cleaved. Complexes of two or more of the analogues,
DB nucleic acids and vectors encoding them may be used alone or in
DB conjunction with each other, for the prevention or treatment of active
DB Factor VIII:C deficiency in a mammal. The analogues may be used as
DB immunogens to raise antibodies, and in the treatment of haemophilias, by
DB improvement of haemostasis. The analogues are resistant to proteolytic
DB cleavage and display increased plasma half-life. They may be administered
DB at lower dosages and by different modes of administration.
DB
DB Sequence 2351 AA:
DB
DB Query Match 100.08; Score 12413; DB 18; Length 2351;
DB Best Local Similarity 100.08; Pred. No. 0;
DB Matches 2350; Conservative 0; Mismatches 1; Indels 0; Gaps 0;
QY 1 MOETSTCFEFLCLRFCSATRRYYGAVELSDMYMQSDLGELPVDARPPRPVPSFPFN 60
DB 1 MOETSTCFEFLCLRFCSATRRYYGAVELSDMYMQSDLGELPVDARPPRPVPSFPFN 60
QY 61 TSVYVKKTLFVEFTDHLFNIAKRPMMGLAPPTQAVYVYVITLKNMAHPSLNAV 120
DB 61 TSVYVKKTLFVEFTDHLFNIAKRPMMGLAPPTQAVYVYVITLKNMAHPSLNAV 120
QY 121 GVSYKASEGAEYDQTSORKEEDKVPFGSGHYTVWOLKENGPAASDPLCLTVSYLSH 180
DB 121 GVSYKASEGAEYDQTSORKEEDKVPFGSGHYTVWOLKENGPAASDPLCLTVSYLSH 180
QY 181 VDLVKNLNSGLIGALVLCRBSGLAKKETQTLKHFLLFAVDECKSHSETNLSLMODRD 240
DB 181 VDLVKNLNSGLIGALVLCRBSGLAKKETQTLKHFLLFAVDECKSHSETNLSLMODRD 240
QY 241 AASARAMPKMTYNGYVNSLPGLICGHRKSYVMYVIGMGTPPVHSIFLEGHTFLVNH 300
DB 241 AASARAMPKMTYNGYVNSLPGLICGHRKSYVMYVIGMGTPPVHSIFLEGHTFLVNH 300
QY 301 ROASLEISPIFFLAQTLMLMDLQFLFLFCHISSHQDGEAYVYKVDSCPEPQLMKKNE 360
DB 301 ROASLEISPIFFLAQTLMLMDLQFLFLFCHISSHQDGEAYVYKVDSCPEPQLMKKNE 360
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301 RASLEISPTIFLTAQFLMLDGLQFLFLCHTSHSQHOGMEAYKVVDSCPEQLBMKNE 360  
Qy 361 EAEYDODDLTJSEMDVYREDDDNSPSFIQIRSVAKKHPKTHWHYIAAEEDMDIAPLVLA 420  
Db 361 EAEYDODDLTJSEMDVYREDDDNSPSFIQIRSVAKKHPKTHWHYIAAEEDMDIAPLVLA 420  
Qy 421 PDRSYKSOYLNNGPORIGRKYKRVFMAAYTDEFKTRREALIQHESGILGPILYGEGDPL 480  
Db 421 PDRSYKSOYLNNGPORIGRKYKRVFMAAYTDEFKTRREALIQHESGILGPILYGEGDPL 480  
Qy 481 LTIIFKNASRPYNTYPIGTTIDVAPLYSRRLPKGVKHLKDPILIGSEIFYKKTATVDEGP 540  
Db 481 LTIIFKNASRPYNTYPIGTTIDVAPLYSRRLPKGVKHLKDPILIGSEIFYKKTATVDEGP 540  
Qy 541 TKSDFRCLTRYSSSEFVNMERDLASGLIGPLLCYKESVDORGNOIMSDKRNVLFSVDE 600  
Db 541 TKSDFRCLTRYSSSEFVNMERDLASGLIGPLLCYKESVDORGNOIMSDKRNVLFSVDE 600  
Qy 601 NRSWYLTENIORFLPNPAGVQLEDEPEFOASNMHSINGYFDSIQVCLHEVAYWYLS 660  
Db 601 NRSWYLTENIORFLPNPAGVQLEDEPEFOASNMHSINGYFDSIQVCLHEVAYWYLS 660  
Qy 661 IGAOTDFLSVFSGTYFKHMYEDTLTLPSPSGEYFPMSENPGLMILGCHNSDFRNG 720  
Db 661 IGAOTDFLSVFSGTYFKHMYEDTLTLPSPSGEYFPMSENPGLMILGCHNSDFRNG 720  
Qy 721 MTALLKVASCDKNTGYYEDSYEDISAVLLSKNNAIEPRSFSONSRHPSTROKOPNATTI 780  
Db 721 MTALLKVASCDKNTGYYEDSYEDISAVLLSKNNAIEPRSFSONSRHPSTROKOPNATTI 780  
Qy 781 PENDIEKTDPMFAHRTMPKIQVSSDPLMLKOSPFGHLSLSLOAKKETEESDPS 840  
Db 781 PENDIEKTDPMFAHRTMPKIQVSSDPLMLKOSPFGHLSLSLOAKKETEESDPS 840  
Qy 841 PGATDSNNSLSBMTNHPROLHSGDMWTFPPESGLOLRNKLCTYATATLKLKLDKYST 900  
Db 841 PGATDSNNSLSBMTNHPROLHSGDMWTFPPESGLOLRNKLCTYATATLKLKLDKYST 900  
Qy 901 SNMLISTIPSDNLACTDNTSLGPPSPMPVHYDSQDPTTLFGKSSPILTESGSPILSEE 960  
Db 901 SNMLISTIPSDNLACTDNTSLGPPSPMPVHYDSQDPTTLFGKSSPILTESGSPILSEE 960  
Qy 961 NNDKSLIESGLMNSGOESMGKNVSTESGRLFFKGRAGHALLTKRNALFKVISILKTN 1020  
Db 961 NNDKSLIESGLMNSGOESMGKNVSTESGRLFFKGRAGHALLTKRNALFKVISILKTN 1020  
Qy 1021 KTSNNSATNRKTHIDGSSLIENSPEWONILIESDTEPKVYTPLIHDRKMLDKNATLRL 1080  
Db 1021 KTSNNSATNRKTHIDGSSLIENSPEWONILIESDTEPKVYTPLIHDRKMLDKNATLRL 1080  
Qy 1081 NMSNKTTSKKNMEMVOQKKEGPIPPDAQNPDMSEFKMLFLPESAWMIQRTGKSNLSNG 1140  
Db 1081 NMSNKTTSKKNMEMVOQKKEGPIPPDAQNPDMSEFKMLFLPESAWMIQRTGKSNLSNG 1140  
Qy 1141 OGSPKOLVSLGPEKSYEGONFLSEKNKYVKGEGFTKDGKLEKMPFSSRNLFLTNIDN 1200  
Db 1141 OGSPKOLVSLGPEKSYEGONFLSEKNKYVKGEGFTKDGKLEKMPFSSRNLFLTNIDN 1200  
Qy 1201 LHENNTHNOEKKIOEELIEKKEKTLIOENNVLPQIHVTGTKNFKNLPFLSTRONEGSYD 1260  
Db 1201 LHENNTHNOEKKIOEELIEKKEKTLIOENNVLPQIHVTGTKNFKNLPFLSTRONEGSYD 1260  
Qy 1261 GAYAPVLODPRLSLDSTNRTKKTTHAFSKGEBEHLGNOJKQIYEYACCTTISNTJ 1320  
Db 1261 GAYAPVLODPRLSLDSTNRTKKTTHAFSKGEBEHLGNOJKQIYEYACCTTISNTJ 1320  
Qy 1321 SOONFVTORSKRALKQFLPLEETLEKRIIVDTSTQMSKNNKHLPTSLTQIDYNEKE 1380  
Db 1321 SOONFVTORSKRALKQFLPLEETLEKRIIVDTSTQMSKNNKHLPTSLTQIDYNEKE 1380  
Qy 1381 KGATQSPPLSDCLTRHSISIPQANRSPLIPIAKVSSPSPRIPIYLRVLPFODNSHLPASY 1440  
Db 1381 KGATQSPPLSDCLTRHSISIPQANRSPLIPIAKVSSPSPRIPIYLRVLPFODNSHLPASY 1440

1441 RKKDSGVESHPLQGAKKNNLSIALITLLEMTGOREVSGLSGTSATNSYTKKYENTVLP 1500  
Db 1441 RKKDSGVESHPLQGAKKNNLSIALITLLEMTGOREVSGLSGTSATNSYTKKYENTVLP 1500  
Qy 1501 KPDLKRTSGKVELLPKVHIYQKDLPEPTESSNGSFGHLDIVSGSLQGTGAIKNEANRP 1560  
Db 1501 KPDLKRTSGKVELLPKVHIYQKDLPEPTESSNGSFGHLDIVSGSLQGTGAIKNEANRP 1560  
Qy 1561 GVPFLVATATESAKPESKLLDPLAMDNHNGYTOJPKDEEMKSQEKSEPKTAFFKKDITLSL 1620  
Db 1561 GVPFLVATATESAKPESKLLDPLAMDNHNGYTOJPKDEEMKSQEKSEPKTAFFKKDITLSL 1620  
Qy 1621 NCESNHAIAAINCGONKPEIETYAKGRTBERLCSQNPVYLKRHORETTRTQSQOE 1680  
Db 1621 NCESNHAIAAINCGONKPEIETYAKGRTBERLCSQNPVYLKRHORETTRTQSQOE 1680  
Qy 1681 IDYDITISVEKKKEDFDIYDEBENOSPPRSFOKTRHYFIAAVERLMDYGMSSSPHYLRNR 1740  
Db 1681 IDYDITISVEKKKEDFDIYDEBENOSPPRSFOKTRHYFIAAVERLMDYGMSSSPHYLRNR 1740  
Qy 1741 AOSGSVPQFKKVVQEPDTSFTQPIYKGBLNEHGLGSPYIAAEVDNIWTFPNQASR 1800  
Db 1741 AOSGSVPQFKKVVQEPDTSFTQPIYKGBLNEHGLGSPYIAAEVDNIWTFPNQASR 1800  
Qy 1801 PYSFYSSLISTEEDQROGAEPRKNEFKVKNETKTYFMKVQHMAPTKDEFCKAMAYPSDV 1860  
Db 1801 PYSFYSSLISTEEDQROGAEPRKNEFKVKNETKTYFMKVQHMAPTKDEFCKAMAYPSDV 1860  
Qy 1861 DLEKDVHSGILGPILVCHNTLNPAGHQVVOYOFALFTIPETKSWYTFENMERNCRA 1920  
Db 1861 DLEKDVHSGILGPILVCHNTLNPAGHQVVOYOFALFTIPETKSWYTFENMERNCRA 1920  
Qy 1921 PCNIOEDPTFKENYRPHALNGYIMDTLPGLVMAODORIRWYLLSGMSNENHSHHSFGH 1980  
Db 1921 PCNIOEDPTFKENYRPHALNGYIMDTLPGLVMAODORIRWYLLSGMSNENHSHHSFGH 1980  
Qy 1981 VFTVRKKEEYKMALYNLYPGVEFVEMLPKAGIMRVCELLIGEHLMAGSTLFLVYSNK 2040  
Db 1981 VFTVRKKEEYKMALYNLYPGVEFVEMLPKAGIMRVCELLIGEHLMAGSTLFLVYSNK 2040  
Qy 2041 QPPLGMASGHTRDQITASGOYQOMAPKLARLHSGSINAMSTRKEPFSWIKVDLAPMII 2100  
Db 2041 QPPLGMASGHTRDQITASGOYQOMAPKLARLHSGSINAMSTRKEPFSWIKVDLAPMII 2100  
Qy 2101 HGKTKQAROKFESSLYISOPTIMYSLDGKKQOTRGNSTGLWVFGVNDSSGIRHNLEN 2160  
Db 2101 HGKTKQAROKFESSLYISOPTIMYSLDGKKQOTRGNSTGLWVFGVNDSSGIRHNLEN 2160  
Qy 2161 PPIIARYIRLHPHYSTRSLRAMELMGCDLNSCAMPJGMEKSAISDAQITASSYPTNMA 2220  
Db 2161 PPIIARYIRLHPHYSTRSLRAMELMGCDLNSCAMPJGMEKSAISDAQITASSYPTNMA 2220  
Qy 2221 TWSPKARLHLOGRSNMROVNVNPEMLQVDFOKTKYAGVTQGVKSLLSMWKFEFL 2280  
Db 2221 TWSPKARLHLOGRSNMROVNVNPEMLQVDFOKTKYAGVTQGVKSLLSMWKFEFL 2280  
Qy 2281 ISSSODGHQMTLFFQNGKAVVFOGNDSTFPVNSLDPPLITRYLRIRHQSVMHIALRM 2340  
Db 2281 ISSSODGHQMTLFFQNGKAVVFOGNDSTFPVNSLDPPLITRYLRIRHQSVMHIALRM 2340  
Qy 2341 EYLGEAODLY 2351  
Db 2341 EYLGEAODLY 2351

RESULT 11  
AAW11425  
ID AAW11425 standard: Protein: 2351 AA.  
XX AAW11425;  
AC  
XX  
DT 20-NOV-1997 (first entry)



1081 NHMSNKTTSKNNMNVQKKEGRIIPDAONPDMSFFKMLFLBESARWIOPTHGKNLSNG 1140  
QY 1141 QGSPKOLVSLGPEKSEVEGONFLSEKNKVVYVGGKEEFGKDVGLKEWVFPSSRNFLTLMDN 1200  
QY 1141 QGSPKOLVSLGPEKSEVEGONFLSEKNKVVYVGGKEEFGKDVGLKEWVFPSSRNFLTLMDN 1200  
QY 1201 LHENNTNHOEKKIOEIELEKKTLLIOENVLYLQIHTYVGNKNEPKNLFLSTROHVESYD 1260  
DB 1201 LHENNTNHOEKKIOEIELEKKTLLIOENVLYLQIHTYVGNKNEPKNLFLSTROHVESYD 1260  
QY 1261 GATAPVLODPRSLNDSTNNTKHTAHESKGEENLELGJGNOTKOIVERKACTTRISPNT 1320  
DB 1261 GATAPVLODPRSLNDSTNNTKHTAHESKGEENLELGJGNOTKOIVERKACTTRISPNT 1320  
QY 1321 SOONFVTOGRKRALKOFRLPLEETELEKRIIVDPTSTOWSKNMKHLTPSTLQIDYNEKE 1380  
DB 1321 SOONFVTOGRKRALKOFRLPLEETELEKRIIVDPTSTOWSKNMKHLTPSTLQIDYNEKE 1380  
QY 1381 KGATOSPISDCLTRSHSISIPQANRSPDIAVSSFPSTIRPIYTLRYLQODNSHLPAASY 1440  
DB 1381 KGATOSPISDCLTRSHSISIPQANRSPDIAVSSFPSTIRPIYTLRYLQODNSHLPAASY 1440  
QY 1441 RKDGSVOESSHFLQAKKNNLSLAITLLEMTGQREVGSLGTSATNSVYTKKVENTVLP 1500  
DB 1441 RKDGSVOESSHFLQAKKNNLSLAITLLEMTGQREVGSLGTSATNSVYTKKVENTVLP 1500  
QY 1501 KPDLPTSGKVELLPKVHIYOKDLPEPTSSNGSGHLDLVESLSLOGTEGAIKNNENRNP 1560  
DB 1501 KPDLPTSGKVELLPKVHIYOKDLPEPTSSNGSGHLDLVESLSLOGTEGAIKNNENRNP 1560  
QY 1561 GVPFRLVATPESAKPRSKLIDLAMDNHGYOIPKEEMKSOQSEPKTAKKKDTLISL 1620  
DB 1561 GVPFRLVATPESAKPRSKLIDLAMDNHGYOIPKEEMKSOQSEPKTAKKKDTLISL 1620  
QY 1621 NACESNHAIAINEGONKPEIEVYTAOKGRTERLCSQNPVLKRHOEITRTTLOSQOEE 1680  
DB 1621 NACESNHAIAINEGONKPEIEVYTAOKGRTERLCSQNPVLKRHOEITRTTLOSQOEE 1680  
QY 1681 IDYDPTISVEKKKEDPIDYDEDENSPSPFOKTRHFFIAAVRLMDYGMSSPHVLRNR 1740  
DB 1681 IDYDPTISVEKKKEDPIDYDEDENSPSPFOKTRHFFIAAVRLMDYGMSSPHVLRNR 1740  
QY 1741 AOSGSVPOFKVYVQETGOSFTQPLRYGELNEHLGLGYIAEVEDNIMWTFRNOASR 1800  
DB 1741 AOSGSVPOFKVYVQETGOSFTQPLRYGELNEHLGLGYIAEVEDNIMWTFRNOASR 1800  
QY 1801 PYSFYSSLISYEEDQOGAEPKRNKFNKPNETKTYFMVQHMAAPTDEFDCKAMAYFSDV 1860  
DB 1801 PYSFYSSLISYEEDQOGAEPKRNKFNKPNETKTYFMVQHMAAPTDEFDCKAMAYFSDV 1860  
QY 1861 DLEKDVHSGLIGPLVCHNTNINPAHGRQVVOEFALFTIFDETSSWYFTEENMERNCRA 1920  
DB 1861 DLEKDVHSGLIGPLVCHNTNINPAHGRQVVOEFALFTIFDETSSWYFTEENMERNCRA 1920  
QY 1921 PCNIOMEDPTFKENYRRAHAINGYIMDTLPGIYMAODORIMWYLLSGMSNENHSHHSFGH 1980  
DB 1921 PCNIOMEDPTFKENYRRAHAINGYIMDTLPGIYMAODORIMWYLLSGMSNENHSHHSFGH 1980  
QY 1981 VFTVARKKEEYKMAIYLYPGVEFTEVEMLPKSAIGIMRECLIGEHLAGKSTLFLVYSNKC 2040  
DB 1981 VFTVARKKEEYKMAIYLYPGVEFTEVEMLPKSAIGIMRECLIGEHLAGKSTLFLVYSNKC 2040  
QY 2041 OPIPLGMASGHTRDQOTASGOYGOMAPKLARLHSSINMWSKPEFSIKVIDLAPIT 2100  
DB 2041 OPIPLGMASGHTRDQOTASGOYGOMAPKLARLHSSINMWSKPEFSIKVIDLAPIT 2100  
QY 2101 HGIKTOGAROKFSSSLYISQFIIMYSIDGKKWQYRGNSTGLTAVFPGVNDSSGIIKHNFN 2160  
DB 2101 HGIKTOGAROKFSSSLYISQFIIMYSIDGKKWQYRGNSTGLTAVFPGVNDSSGIIKHNFN 2160  
QY 2161 PPIIARYIRLHPHYISRSTLRMELMGCDLNSCNPJGMSKAIISAOITASTASYTNMFA 2220  
DB 2161 PPIIARYIRLHPHYISRSTLRMELMGCDLNSCNPJGMSKAIISAOITASTASYTNMFA 2220

QY 2221 TWSPSKARLHLQGRSNAWRPOVNNKPEMLQVDFOKTMKVTGVTGQVSKLLTSMYKEFL 2280  
DB 2221 TWSPSKARLHLQGRSNAWRPOVNNKPEMLQVDFOKTMKVTGVTGQVSKLLTSMYKEFL 2280  
QY 2281 ISSODGHQWTLFFQNGKVKYVQGNQDSFTPVVNSLDPLLRIRYLRHPQSWHQIALRM 2340  
DB 2281 ISSODGHQWTLFFQNGKVKYVQGNQDSFTPVVNSLDPLLRIRYLRHPQSWHQIALRM 2340  
QY 2341 EYLGCSEAODLY 2351  
DB 2341 EYLGCSEAODLY 2351  
RESULT 12  
AAW11419  
ID AAW11419 standard; Protein: 2351 AA.  
XX  
AC AAW11419;  
XX  
DT 20-NOV-1997 (first entry)  
XX  
DE Active Factor VIII:C analogue, delta 1311, + Pro insertion.  
XX  
KW Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;  
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KW plasma protease; thrombin; immunogen; antibody; haemophilia; therapy;  
KW proteolytic cleavage.  
XX  
OS Homo sapiens.  
OS Synthetic.  
XX  
FH Key  
FT peptide  
FT /note= "signal peptide"  
FT Protein  
FT /note= "mature Factor VIII:C"  
FT Region  
FT /note= "heavy chain fragment"  
FT Misc-difference 1329..1330  
FT /note= "site of 1 residue deletion"  
FT Modified-site 1330  
FT /note= "inserted residue"  
FT Region 1668..2350  
FT /note= "light chain fragment"  
FT Domain 760..1667  
FT /note= "B domain"  
PN WO9703195-A1.  
XX  
PD 30-JAN-1997.  
XX  
PF 09-JUL-1996; 96WO-US11444.  
XX  
PR 11-JUL-1995; 95US-0001025.  
XX  
PA (CHIR ) CHIRON CORP.  
PI Cohen FE, Hung DT, Innis M;  
DR WPI; 1997-119050/11.  
XX  
PT Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophilias, by improvement of  
FT haemostasis  
XX  
PS Claim 27; Page -: 90pp; English.  
XX  
CC AAW11330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg



CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophiliacs, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.

XX Sequence 2351 AA:  
SQ

Query Match 100.0%; Score 12413; DB 18; Length 2351;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2350; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 1 MOELSTCFCLLRPCSATPRRYTGAVELSMQSDGLGFLPDAFPPRPVKSPPN 60  
DB 1 MOELSTCFCLLRPCSATPRRYTGAVELSMQSDGLGFLPDAFPPRPVKSPPN 60  
QY 61 TSVYKKTFLFEPTDHLFNIAKRPVWGLGPT10AEVYDFVTITLKMAASHPVSLHAV 120  
DB 61 TSVYKKTFLFEPTDHLFNIAKRPVWGLGPT10AEVYDFVTITLKMAASHPVSLHAV 120  
QY 121 GSVYWKASGAEYDDQTSQREKEDKVPFGSGHTYVQVLEKNGPMASDPLCTLYSLSH 180  
DB 121 GSVYWKASGAEYDDQTSQREKEDKVPFGSGHTYVQVLEKNGPMASDPLCTLYSLSH 180  
QY 181 VDLKXDLNSGLIGALLVCRESGLAEKQTLNHPFLLFAVPDEGKSMSEPKNSLMQDD 240  
DB 181 VDLKXDLNSGLIGALLVCRESGLAEKQTLNHPFLLFAVPDEGKSMSEPKNSLMQDD 240  
QY 241 AASARAMPKMHYVNGVYNSLEPGLIGCHRSVYTHVYIGMCTPEVHSTFEEGRTFLVRNH 300  
DB 241 AASARAMPKMHYVNGVYNSLEPGLIGCHRSVYTHVYIGMCTPEVHSTFEEGRTFLVRNH 300  
QY 301 RQASLEISPTFLTAOTLLMDGOFLEFCHISSHOHGMEAVYKVDSCPEEPQIRMKNE 360  
DB 301 RQASLEISPTFLTAOTLLMDGOFLEFCHISSHOHGMEAVYKVDSCPEEPQIRMKNE 360  
QY 361 EAEDYDDDLTDSMDVVRFDNDSPSFTQIRSAVAKKHPTWVHYIAAEEEDMDYAPLVJA 420  
DB 361 EAEDYDDDLTDSMDVVRFDNDSPSFTQIRSAVAKKHPTWVHYIAAEEEDMDYAPLVJA 420  
QY 421 PDDRSYKSOYLNGSPQIRGKRYKRYRMAKYRDEFTKRRALQHBEGITGLLYGEGDPL 480  
DB 421 PDDRSYKSOYLNGSPQIRGKRYKRYRMAKYRDEFTKRRALQHBEGITGLLYGEGDPL 480  
QY 481 LTIFFKNOASRPYNIYRPHGITDVRPLYSRRLPKGVKHLKDPILPEEIFRYKWTYVEDGF 540  
DB 481 LTIFFKNOASRPYNIYRPHGITDVRPLYSRRLPKGVKHLKDPILPEEIFRYKWTYVEDGF 540  
QY 541 TKSDFPCLTRYSSPFNMERDLASGLIPLLICVKESVDQRGNOQMSKRVNLIFFSVFDE 600  
DB 541 TKSDFPCLTRYSSPFNMERDLASGLIPLLICVKESVDQRGNOQMSKRVNLIFFSVFDE 600  
QY 601 NRSWLTENTORFLPMPAGVOLEDEPEROASIMHSTNGVYPSILOSLYCLEHVAWYVILS 660  
DB 601 NRSWLTENTORFLPMPAGVOLEDEPEROASIMHSTNGVYPSILOSLYCLEHVAWYVILS 660  
QY 661 IGAQTDLSVFSGTYFFKHKWYEDTLTLFPESGETVFMSEMPGLMILGCHNSDFRNNG 720  
DB 661 IGAQTDLSVFSGTYFFKHKWYEDTLTLFPESGETVFMSEMPGLMILGCHNSDFRNNG 720  
QY 721 WTALKVSSCDKMTGDIYEDSYEDISAYLISKNAIEPRFSQNSRHSPTROKOFNATYI 780  
DB 721 WTALKVSSCDKMTGDIYEDSYEDISAYLISKNAIEPRFSQNSRHSPTROKOFNATYI 780

QY 781 PENDIEKTPWFAHRTPMFKIOWNSSDILLMLRQSPRHGLSLDLOEAKYEFESDPS 840  
DB 781 PENDIEKTPWFAHRTPMFKIOWNSSDILLMLRQSPRHGLSLDLOEAKYEFESDPS 840  
QY 841 PGATIDNSNSLSMTHFRPOLHSGDWYFPESGLDRLNKLGTATATELKLIDKRVST 900  
DB 841 PGATIDNSNSLSMTHFRPOLHSGDWYFPESGLDRLNKLGTATATELKLIDKRVST 900  
QY 901 SNNLITSPSDMLAAGTNTSSLCPPSPHVDLSQDPTLLGKSSPTRESGPTLSLEE 960  
DB 901 SNNLITSPSDMLAAGTNTSSLCPPSPHVDLSQDPTLLGKSSPTRESGPTLSLEE 960  
QY 961 NNDSKLIESGLNISOESSMCKNVSSTESGFLRKGRAHGAPALLTKDNALFKVYSILATN 1020  
DB 961 NNDSKLIESGLNISOESSMCKNVSSTESGFLRKGRAHGAPALLTKDNALFKVYSILATN 1020  
QY 1021 KTSNNSATNRKTHIDGSLILIENTSPWQNIIESDTEKRYTPLIHDMIMDKNATATRL 1080  
DB 1021 KTSNNSATNRKTHIDGSLILIENTSPWQNIIESDTEKRYTPLIHDMIMDKNATATRL 1080  
QY 1081 NMSNKTSSKNMEVQOKKEGPIPPDAQNPMSPEFKMLFIPESARIQTHGKNSLNSG 1140  
DB 1081 NMSNKTSSKNMEVQOKKEGPIPPDAQNPMSPEFKMLFIPESARIQTHGKNSLNSG 1140  
QY 1141 QGSPKOLVSLGPEKSVBQNFLEKKNVYVGKEFTYDGLAKEMVFPSSRNLFETNIDN 1200  
DB 1141 QGSPKOLVSLGPEKSVBQNFLEKKNVYVGKEFTYDGLAKEMVFPSSRNLFETNIDN 1200  
QY 1201 LHENNTHNOEKKLOEIEKKEETLLOENVVLPQIHVTGTKNFMKNLFLSTRONVEGSD 1260  
DB 1201 LHENNTHNOEKKLOEIEKKEETLLOENVVLPQIHVTGTKNFMKNLFLSTRONVEGSD 1260  
QY 1261 GAYAPVLOPFRSLNDSTNRKTHAHFSSKKEEENLEGGNOTQOIEYKACTRISPT 1320  
DB 1261 GAYAPVLOPFRSLNDSTNRKTHAHFSSKKEEENLEGGNOTQOIEYKACTRISPT 1320  
QY 1321 SQONFYQSKALKQOFPLLELELEKRIYDPTSTQSKNMKHLTPSTLQIDYNEKE 1380  
DB 1321 SQONFYQSKALKQOFPLLELELEKRIYDPTSTQSKNMKHLTPSTLQIDYNEKE 1380  
QY 1381 KGALTOSSDCLTRSHSIPOANRSPPLIAKVSSPSPRIYTLRVLPDONSHTLPASY 1440  
DB 1381 KGALTOSSDCLTRSHSIPOANRSPPLIAKVSSPSPRIYTLRVLPDONSHTLPASY 1440  
QY 1441 RKDSGVQESSHFLQGAKKNNLSAILTLEMTGDQREVGSLGTSATNSVYKKVEKTVLP 1500  
DB 1441 RKDSGVQESSHFLQGAKKNNLSAILTLEMTGDQREVGSLGTSATNSVYKKVEKTVLP 1500  
QY 1501 KPDLPTSGKVELLRKVIH YOKDLFPTETNSGPGHLDLVGSSILQGTBGAIKWNEANRP 1560  
DB 1501 KPDLPTSGKVELLRKVIH YOKDLFPTETNSGPGHLDLVGSSILQGTBGAIKWNEANRP 1560  
QY 1561 GKVPFLVATESSAKTPSKLLDPLAMDNIHGTQIPKEEMKSOEKSPEKTAFFKKKDTIISL 1620  
DB 1561 GKVPFLVATESSAKTPSKLLDPLAMDNIHGTQIPKEEMKSOEKSPEKTAFFKKKDTIISL 1620  
QY 1621 NACESNHAIAINEGQNPBEIEVYMAKOGTERLCSQNPVLKRRHOEIRTRTLOSDEE 1680  
DB 1621 NACESNHAIAINEGQNPBEIEVYMAKOGTERLCSQNPVLKRRHOEIRTRTLOSDEE 1680  
QY 1681 IDYDDTISVPMKKEPDIYDDENQSRSPQKTRHYFAAVERLMYMGSSPHYLRNR 1740  
DB 1681 IDYDDTISVPMKKEPDIYDDENQSRSPQKTRHYFAAVERLMYMGSSPHYLRNR 1740  
QY 1741 AOGSGVQFKKYYFOEFTDGSFTQPLRGLNHLGLGPTIYRAVEDNIMVYFRQOASR 1800  
DB 1741 AOGSGVQFKKYYFOEFTDGSFTQPLRGLNHLGLGPTIYRAVEDNIMVYFRQOASR 1800  
QY 1801 PYFSYSLISYEDDROGAEBPRKNFVKNPTKTYFWKVQHHMPTKDEPCKAMAVFSOV 1860  
DB 1801 PYFSYSLISYEDDROGAEBPRKNFVKNPTKTYFWKVQHHMPTKDEPCKAMAVFSOV 1860

QY 1861 DLEKDVHSGLIIGPLVCHNTNLPNAHGRVYVOEFALFTTIPDETKEWYFTENNERNCR 1920  
DB 1861 DLEKDVHSGLIIGPLVCHNTNLPNAHGRVYVOEFALFTTIPDETKEWYFTENNERNCR 1920  
QY 1921 PCNIOMEDPTEKENYEFNAHNGYIMDTLPGVNAOQORIRAWLISMSGNEHSHIFPSH 1980  
DB 1921 PCNIOMEDPTEKENYEFNAHNGYIMDTLPGVNAOQORIRAWLISMSGNEHSHIFPSH 1980  
QY 1981 VFTVRKKEEYKALVLYPGVEFVEMLPKAGIMRECLIGEHLMAGMSTLELVYSNKC 2040  
DB 1981 VFTVRKKEEYKALVLYPGVEFVEMLPKAGIMRECLIGEHLMAGMSTLELVYSNKC 2040  
QY 2041 QTPLGMAHGHIRDFQITASGYGOMAPKLARLHSGSINAMSTKEPFSWIKVDLAPMII 2100  
DB 2041 QTPLGMAHGHIRDFQITASGYGOMAPKLARLHSGSINAMSTKEPFSWIKVDLAPMII 2100  
QY 2101 HGITOGAROKFSSLYISQFIIMYSIDGKKMOTYRGNSGTLMFPGVDSGKININ 2160  
DB 2101 HGITOGAROKFSSLYISQFIIMYSIDGKKMOTYRGNSGTLMFPGVDSGKININ 2160  
QY 2161 PPIIARTIRLHPHYSINSTRLMELMCCDINSMPPLGMSKALSDAOITASSYFTNMFA 2220  
DB 2161 PPIIARTIRLHPHYSINSTRLMELMCCDINSMPPLGMSKALSDAOITASSYFTNMFA 2220  
QY 2221 TWSPSKARLHLOGRSNAMPPOVNNPKEMLVDFOKTMKVTGVTQGVKSLLTSMYKEFL 2280  
DB 2221 TWSPSKARLHLOGRSNAMPPOVNNPKEMLVDFOKTMKVTGVTQGVKSLLTSMYKEFL 2280  
QY 2281 ISSQDGHQWTLTFPONGKVKYFQGNODSPFPVYNSLDPLRLRYRIHPQSWHQAIALRM 2340  
DB 2281 ISSQDGHQWTLTFPONGKVKYFQGNODSPFPVYNSLDPLRLRYRIHPQSWHQAIALRM 2340  
QY 2341 EYLCEAODLY 2351  
DB 2341 EYLCEAODLY 2351

RESULT 13  
AAW11398  
ID AAW11398 standard; Protein: 2351 AA.  
XX  
AC AAW11398;  
XX  
DT 18-NOV-1997 (first entry)  
XX

DE Active Factor VIII:C analogue, delta 746, + residue 746 insertion.  
XX  
KM Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;  
KM fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KW plasma; protease; thrombin; immunogen; antibody; haemophilic; therapy;  
KW proteolytic cleavage.  
XX  
OS Homo sapiens.  
OS Synthetic.  
XX  
FX  
XX  
FT Key Location/Qualifiers  
FT Peptide 1..19  
FT Protein /note= "signal peptide"  
FT Protein 20..2351  
FT Region /note= "mature Factor VIII:C"  
FT Region 20..1667  
FT Misc-difference 744..765 /note= "heavy chain fragment"  
FT /note= "site of 1 residue deletion"  
FT Modified-site 765  
FT /note= "inserted residue"  
FT Region 1668..2350  
FT /note= "light chain fragment"  
FT Domain 760..1667  
FT /note= "B domain"  
XX  
PN MO9703195-A1.  
XX

PD 30-JAN-1997.  
XX  
PF 09-JUL-1996; 96MO-US1444.  
XX  
PR 11-JUL-1995; 95US-0001025.  
XX  
PA (CHIR ) CHIRON CORP.  
XX  
PI Cohen FE, Hung DF, Innis M;  
XX  
DR WPI; 1997-119050/11.  
XX  
PT Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophilias, by improvement of  
PS haemostasis  
XX  
PS Claim 23; Page -: 90pp; English.  
XX  
CC AAW11330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophilias, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX  
XX  
SO Sequence 2351 AA;

Query Match 100.0%; Score 12413; DB 18; Length 2351;  
Best Local Similarity 100.0%; Pred No 0;  
Matches 2350; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 1 M0E1STCFPLCLRFCEFSATRRYYLGAVELSMDYQSDGLPLVDARPPRVRKSPFPN 60  
DB 1 M0E1STCFPLCLRFCEFSATRRYYLGAVELSMDYQSDGLPLVDARPPRVRKSPFPN 60  
QY 61 TSVVYKKTLEFEFTDHLFNIAKPRPPMGLGPTLOAEVYDVTVITLKNMASHPVSLHAV 120  
DB 61 TSVVYKKTLEFEFTDHLFNIAKPRPPMGLGPTLOAEVYDVTVITLKNMASHPVSLHAV 120  
QY 121 GVSYKASGAEYDDQTSOREKDDKVPFGSGHYYWQVAKENGPASPLCLTYSTLSH 180  
DB 121 GVSYKASGAEYDDQTSOREKDDKVPFGSGHYYWQVAKENGPASPLCLTYSTLSH 180  
QY 181 VDLVYDNLNGLIALYLCREGSLAKKQYOTLHKFTLLFANFDEGKSMHSETKNSLMODRD 240  
DB 181 VDLVYDNLNGLIALYLCREGSLAKKQYOTLHKFTLLFANFDEGKSMHSETKNSLMODRD 240  
QY 241 AASARAMPKMTVNGYVNRSLPGLICGHRKSVYVHWIGMTPEVHSIFLEGHTFLVNNH 300  
DB 241 AASARAMPKMTVNGYVNRSLPGLICGHRKSVYVHWIGMTPEVHSIFLEGHTFLVNNH 300  
QY 301 RQASLEISPIITFLAQTLLMDLQOFLTFCGHISSHOHGMGAAYKVDSCPEEPOLRMKNNE 360  
DB 301 RQASLEISPIITFLAQTLLMDLQOFLTFCGHISSHOHGMGAAYKVDSCPEEPOLRMKNNE 360  
QY 361 EAEYDDDLTDSMDVYRFPDDNSPSFQIISVAKKPKTWHTYIAAEEEDMDAPLVLA 420  
DB 361 EAEYDDDLTDSMDVYRFPDDNSPSFQIISVAKKPKTWHTYIAAEEEDMDAPLVLA 420

Qy	421	DDDSKYSQYLNNGQRIQGRKKKVRMAVTDERTKTRBAIQHSSGILGRLYXGCGTL	480
Dd	421	PDDSTKSYQLNNGQRIQGRKKKVRMAVTDERTKTRBAIQHSSGILGRLYXGCGTL	480
Qy	481	LIFRNOASRPNIYPHGITDVRPLYSRRLPKGVKHLDPFLIBGELTFKKMYVEGCP	540
Dd	481	LIFRNOASRPNIYPHGITDVRPLYSRRLPKGVKHLDPFLIBGELTFKKMYVEGCP	540
Qy	541	TKSDPRLCTRYVYSFYNMNERDLASGLIGLPLCTCYKESYDQGNQIMSDKRNVLFEVDE	600
Dd	541	TKSDPRLCTRYVYSFYNMNERDLASGLIGLPLCTCYKESYDQGNQIMSDKRNVLFEVDE	600
Qy	601	NRSWYLFENQRIPLRPPGVQLEDPEEQASINMHSINCYVDSIQLSVCHBAVAYTIS	660
Dd	601	NRSWYLFENQRIPLRPPGVQLEDPEEQASINMHSINCYVDSIQLSVCHBAVAYTIS	660
Qy	661	IGAOTDLSAFPSGTYFFKKMYEDTLTFPSGGEVFNKSNBNGMLICLCHNSDPNRNG	720
Dd	661	IGAOTDLSAFPSGTYFFKKMYEDTLTFPSGGEVFNKSNBNGMLICLCHNSDPNRNG	720
Qy	721	MTALLKYSCKDKWGDYEDSEDIISAYLLSKNNAIEPSPSONSRHPSTROKQFNATTI	780
Dd	721	MTALLKYSCKDKWGDYEDSEDIISAYLLSKNNAIEPSPSONSRHPSTROKQFNATTI	780
Qy	781	PENDIEKTDWFMHRTPMKIQNVSSDDLMLTROSPHIGLSLSDQEKYETFDSDPS	840
Dd	781	PENDIEKTDWFMHRTPMKIQNVSSDDLMLTROSPHIGLSLSDQEKYETFDSDPS	840
Qy	841	PGALDSNNSLSEMTHRPQLHHSQDMVFPESGLOJRLNEKIGTATATKLIDFVSVST	900
Dd	841	PGALDSNNSLSEMTHRPQLHHSQDMVFPESGLOJRLNEKIGTATATKLIDFVSVST	900
Qy	901	SNNLITIPEDNLAAGTOWTSISGRPMAPHYNSOJTLTKXKSSPLTSGGSLSLSE	960
Dd	901	SNNLITIPEDNLAAGTOWTSISGRPMAPHYNSOJTLTKXKSSPLTSGGSLSLSE	960
Qy	961	NNDSKLLIESGLMNSOESSGKNKWSSTSGRLFGRKRAHPALTRKIDNALRKVYSILKTN	1020
Dd	961	NNDSKLLIESGLMNSOESSGKNKWSSTSGRLFGRKRAHPALTRKIDNALRKVYSILKTN	1020
Qy	1021	KTSNNSATNKRTHIDGSPSLLENPSYWNQILLESDEFFKVPYPLIHBMRLMDNATRL	1080
Dd	1021	KTSNNSATNKRTHIDGSPSLLENPSYWNQILLESDEFFKVPYPLIHBMRLMDNATRL	1080
Qy	1081	NHMSKRTTSSKNMEMYQOKKEGPIPPDQNPDMSPFKMLFLPESARWORTHKNSLNG	1140
Dd	1081	NHMSKRTTSSKNMEMYQOKKEGPIPPDQNPDMSPFKMLFLPESARWORTHKNSLNG	1140
Qy	1141	OGSPRKOVLALGEXKVECONFLSKKNVYVGGEGFTKQYGLKEVPSRNPLFLNND	1200
Dd	1141	OGSPRKOVLALGEXKVECONFLSKKNVYVGGEGFTKQYGLKEVPSRNPLFLNND	1200
Qy	1201	LHNNTHNOEKIJOELIEKKEPLLQOENVLPQIHVYTGKFNKMLPILSTRONVEGSTD	1260
Dd	1201	LHNNTHNOEKIJOELIEKKEPLLQOENVLPQIHVYTGKFNKMLPILSTRONVEGSTD	1260
Qy	1261	GAYAPVLODPRSLNDSTNTTKKHTAHESKSGEENELGJGNTOKIYEKACTTRISPT	1320
Dd	1261	GAYAPVLODPRSLNDSTNTTKKHTAHESKSGEENELGJGNTOKIYEKACTTRISPT	1320
Qy	1321	SOQNPVYQSRKALNKFRLPEETLEKRIYVDJSTQSKMMKMLPSTLTQIDNENE	1380
Dd	1321	SOQNPVYQSRKALNKFRLPEETLEKRIYVDJSTQSKMMKMLPSTLTQIDNENE	1380
Qy	1381	KGATIOSPLSDCTBRSHTSIPQANSPLPIAKVSSPSTIRYITRVLVFOONSSHPLAASY	1440
Dd	1381	KGATIOSPLSDCTBRSHTSIPQANSPLPIAKVSSPSTIRYITRVLVFOONSSHPLAASY	1440
Qy	1441	RKKSQVOESSHFLVQAKAKNNLSIALITLLEMTDQOREVSGISGTSATNSVYKKEVENTVLP	1500
Dd	1441	RKKSQVOESSHFLVQAKAKNNLSIALITLLEMTDQOREVSGISGTSATNSVYKKEVENTVLP	1500
Qy	1501	KFDLPKTSKSGVELLPVNIHYQKDLFPPTETSNQSPGLDLYVESLSLOGBEAIKMNANPMP	1560

Db	1501	KPDLPKTSQVAVLLPVRVHYIYOKDLPPETETSGSPGHLDVBSGLDGTSEAIKKNENANRP	1560
Oy	1561	GKVPPLVATVATSSAKTPSKLDDPLAMDNHYGTQIQKEEMKSOEKSPKTAFFKKKDTIISL	1620
Db	1561	GKVPPLVATVATSSAKTPSKLDDPLAMDNHYGTQIQKEEMKSOEKSPKTAFFKKKDTIISL	1620
Oy	1621	NACESNHAIAINIEGONKKEIEIVTWAGOGTETELCSQNPVYLKRRHOEIRTRTLASDOEE	1680
Db	1621	NACESNHAIAINIEGONKKEIEIVTWAGOGTETELCSQNPVYLKRRHOEIRTRTLASDOEE	1680
Oy	1681	IDYDDTTSVEMKKEDPDIDEDENQSPESFOKTRHVFIAAVERLMAYGSSSPHYLNR	1740
Db	1681	IDYDDTTSVEMKKEDPDIDEDENQSPESFOKTRHVFIAAVERLMAYGSSSPHYLNR	1740
Oy	1741	AOSGSVPOFKKVFQFQETPGSTFQPIVIRGELNBNHLLGLPYRAEVEDNIMVTFRRQASR	1800
Db	1741	AOSGSVPOFKKVFQFQETPGSTFQPIVIRGELNBNHLLGLPYRAEVEDNIMVTFRRQASR	1800
Oy	1801	PVSEYSSLSIYEDDQROGAEPRKNFVKPNETKTYFAKVQHNHMAPTKDFDCKAMAFESVY	1860
Db	1801	PVSEYSSLSIYEDDQROGAEPRKNFVKPNETKTYFAKVQHNHMAPTKDFDCKAMAFESVY	1860
Oy	1861	DLEKDVHSGILIGLVLCHNTLNPAGROYTVQEFLLFTIFDETKSYETENMERNCRA	1920
Db	1861	DLEKDVHSGILIGLVLCHNTLNPAGROYTVQEFLLFTIFDETKSYETENMERNCRA	1920
Oy	1921	PCNIQMEDPFFKENVFPAHINQYIMDTLPGLVMAQOQIRIWTLLSMGSENIHSIHFSGH	1980
Db	1921	PCNIQMEDPFFKENVFPAHINQYIMDTLPGLVMAQOQIRIWTLLSMGSENIHSIHFSGH	1980
Oy	1981	VETVARKKEEYKMAIYNLYPGVEEYEMLPKSAQIMVBEILLJGHNHAGNSTLFLYVSNQC	2040
Db	1981	VETVARKKEEYKMAIYNLYPGVEEYEMLPKSAQIMVBEILLJGHNHAGNSTLFLYVSNQC	2040
Oy	2041	QTPPLGMASGHTRPQTTASGQYGGMAFPLARLHSSSIANASTKEPSPYKIKVULLAPMII	2100
Db	2041	QTPPLGMASGHTRPQTTASGQYGGMAFPLARLHSSSIANASTKEPSPYKIKVULLAPMII	2100
Oy	2101	HGIKTQGAROKFESSLYISOFTIMYSLDGKKWQYIRGNSTGTLMEFGVNDSSGIRKHNIN	2160
Db	2101	HGIKTQGAROKFESSLYISOFTIMYSLDGKKWQYIRGNSTGTLMEFGVNDSSGIRKHNIN	2160
Oy	2161	PLIIRYRRLPHYHSIRSTLRMEIEMGCDLNSGSMPLGMSKAISDAQITASSXYTNMFA	2220
Db	2161	PLIIRYRRLPHYHSIRSTLRMEIEMGCDLNSGSMPLGMSKAISDAQITASSXYTNMFA	2220
Oy	2221	TWSPSKATLHJGGSNAMPROYNNKPEMLQYDQCKTMKYTGTTQGVSLTISMYKEPL	2280
Db	2221	TWSPSKATLHJGGSNAMPROYNNKPEMLQYDQCKTMKYTGTTQGVSLTISMYKEPL	2280
Oy	2281	ISSSDQGHQWTLFQNGKAKVYVQGNQDSFTPVNNSLDPLLRIRLRHPOSHWQIALQMA	2340
Db	2281	ISSSDQGHQWTLFQNGKAKVYVQGNQDSFTPVNNSLDPLLRIRLRHPOSHWQIALQMA	2340
Oy	2341	EVLGCEADQDLY 2351	
Db	2341	EVLGCEADQDLY 2351	
RESULT 14			
AAAM1387			
ID	AAAM1387	standard; Protein; 2351 AA.	
XX	AAAM1387;		
XX	18-NOV-1997	(first entry)	
DE	Active Factor VIII:C analogue N357X.		
XX	Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;		
KW	fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;		
KM	plasma protease; thrombin; immunogen; antibody; haemophilic therapy;		

KM	proteolytic cleavage.
XX	
OS	Homo sapiens.
OS	Synthetic.
XX	
PH	Key
FT	Location/Qualifiers
FT	1..19
FT	/note="signal peptide"
FT	20..2351
FT	Protein
FT	/note="mature Factor VIII:C"
FT	20..1667
FT	Region
FT	/note="heavy chain fragment"
FT	376
FT	Modified-site
FT	/label="Phe, Glu, Pro
FT	1668..2350
FT	Region
FT	/note="light chain fragment"
FT	760..1667
FT	Domain
FT	/note="B domain"
XX	
PN	MO9703195-A1.
XX	
PD	30-JAN-1997.
XX	
PE	09-JUL-1996; 96MO-US11444.
XX	
PR	11-JUL-1995; 95US-0001025.
XX	
PA	(CHIR ) CHIRON CORP.
XX	
PI	Cohen FE, Hung DT, Innis M;
XX	
DR	WPI; 1997-119050/11.
XX	
PT	Factor VIII:C analog modified adjacent to a non-activating Arg
PT	residue - used in the treatment of haemophiliacs, by improvement of
PT	hemostasis
XX	
PS	Claim 20; Page -: 90pp; English.
XX	
CC	AA11330-W11472 represent active Factor VIII:C analogues of the
CC	invention. These sequences were created by mutating the wild type Factor
CC	VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC	analogues comprise a native Factor VIII:C polypeptide modified at a site
CC	adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC	dipeptide is created. Factor VIII:C is a large glycoprotein that
CC	participates in the blood coagulation cascade that ultimately converts
CC	soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC	deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC	X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC	activated by plasma proteases, such as thrombin. During activation the
CC	mature polypeptide is cleaved to generate heavy and light chain fragments
CC	that are further cleaved. Complexes of two or more of the analogues,
CC	nucleic acids and vectors encoding them may be used alone or in
CC	conjunction with each other for the prevention or treatment of active
CC	Factor VIII:C deficiency in a mammal. The analogues may be used as
CC	immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC	improvement of haemostasis. The analogues are resistant to proteolytic
CC	cleavage and display increased plasma half-life. They may be administered
CC	at lower dosages and by different modes of administration.
XX	
SQ	Sequence 2351 AA:
Query Match	100.0%; Score 12413; DB 18; Length 2351;
Best Local Similarity	100.0%; Pred. No. 0;
Matches 2350; Conservative	0; Mismatches 1; Indels 0; Gaps 0;
QY	1 MQEISTCFCLIRCFSAIRRYLGAVELSMYQSDLGELPVDARPPRVKSPFN 60
DB	1 MQEISTCFCLIRCFSAIRRYLGAVELSMYQSDLGELPVDARPPRVKSPFN 60
QY	61 TSVVYKKTLEVEFDHLFNIAKPRPPMGLGPTIOAEVYDVVITLKMASSHVSLHAY 120
DB	61 TSVVYKKTLEVEFDHLFNIAKPRPPMGLGPTIOAEVYDVVITLKMASSHVSLHAY 120

QY	121 GSVYWKASGAEYDDQTSOREKEDDKVPCGSHTYVWYLAKEGPMASDPLCLTYSLSH 180
DB	121 GSVYWKASGAEYDDQTSOREKEDDKVPCGSHTYVWYLAKEGPMASDPLCLTYSLSH 180
QY	181 VDLVKDINSGLIGALLVCREGSLAKKKTOTLHKFTLLFAYVDEKSMHSETKNSLMODRD 240
DB	181 VDLVKDINSGLIGALLVCREGSLAKKKTOTLHKFTLLFAYVDEKSMHSETKNSLMODRD 240
QY	241 AASARAMPKMTVNGVYNSLPGLIGCHRSYVMHVGMTTPEVHSTFLBGTFTLVRNH 300
DB	241 AASARAMPKMTVNGVYNSLPGLIGCHRSYVMHVGMTTPEVHSTFLBGTFTLVRNH 300
QY	301 RQASLEISPTFTLTAQTLTLMIDGQFLFCHISSHQDGEAVYKVDSCPEEPOLRMKNNE 360
DB	301 RQASLEISPTFTLTAQTLTLMIDGQFLFCHISSHQDGEAVYKVDSCPEEPOLRMKNNE 360
QY	361 EAEYDDDLTDSMDVYRFPDDNSPFTQIRSAKKNPKTWYHIAAEEDMDYAPLVLA 420
DB	361 EAEYDDDLTDSMDVYRFPDDNSPFTQIRSAKKNPKTWYHIAAEEDMDYAPLVLA 420
QY	421 PDDRSYKSOYLANNGPQRIGRKKYKRVEMAYTDEFTKRAIQHESGILGPLYGEVDTL 480
DB	421 PDDRSYKSOYLANNGPQRIGRKKYKRVEMAYTDEFTKRAIQHESGILGPLYGEVDTL 480
QY	481 LIIFKNQASRPNIYPHGITDVRPLYSRRLPKGVKHLKDFLLPGEIFKRYMTVTEDEP 540
DB	481 LIIFKNQASRPNIYPHGITDVRPLYSRRLPKGVKHLKDFLLPGEIFKRYMTVTEDEP 540
QY	541 TKSDPCLTPTYSAPFNMERDLASGLIGPLITCYKESVQORNOJMSDKRNVILFVPE 600
DB	541 TKSDPCLTPTYSAPFNMERDLASGLIGPLITCYKESVQORNOJMSDKRNVILFVPE 600
QY	601 NRSWYLTENTQRLPNPACVOLDEPEFOASINHSINGVYEDSLQSLCYLAEVAYVILS 660
DB	601 NRSWYLTENTQRLPNPACVOLDEPEFOASINHSINGVYEDSLQSLCYLAEVAYVILS 660
QY	661 IGAOTDELVSFFSGYFFKHKWYEDTTLTLPFSGEIVFMSMENPGLMILGCHNSDRNNG 720
DB	661 IGAOTDELVSFFSGYFFKHKWYEDTTLTLPFSGEIVFMSMENPGLMILGCHNSDRNNG 720
QY	721 MTALLKVSQCDKNTGTYEDSEDIASVILSKNNALIEPFSQNSRHPSTROQFNATTT 780
DB	721 MTALLKVSQCDKNTGTYEDSEDIASVILSKNNALIEPFSQNSRHPSTROQFNATTT 780
QY	781 PENDIEKTDPEFAHRTPMFKIQONVSSDLMILROSPTRHGILSLDQEAKEYTFSDPS 840
DB	781 PENDIEKTDPEFAHRTPMFKIQONVSSDLMILROSPTRHGILSLDQEAKEYTFSDPS 840
QY	841 PGALDSNNSLSEMTTHRPQLHHSQDMVTFPESGLOLRLEKLGTTAATELKKLDFKVSST 900
DB	841 PGALDSNNSLSEMTTHRPQLHHSQDMVTFPESGLOLRLEKLGTTAATELKKLDFKVSST 900
QY	901 SNNLISITPESDNLAAOTDNTSSLAGPSPMAYHYOSODTLTLPFKSSPPLTESGGLSSE 960
DB	901 SNNLISITPESDNLAAOTDNTSSLAGPSPMAYHYOSODTLTLPFKSSPPLTESGGLSSE 960
QY	961 NNDKSLLESGLMNSQSSGKKNVSTESGRLFGKRAHPALLITDONALFKVSTSLTKTN 1020
DB	961 NNDKSLLESGLMNSQSSGKKNVSTESGRLFGKRAHPALLITDONALFKVSTSLTKTN 1020
QY	1021 KTSNNSATNKRTHIDPSLLIENSFPVQNTLSDPEFKKVTPLIHDHMLDKKNAATLRL 1080
DB	1021 KTSNNSATNKRTHIDPSLLIENSFPVQNTLSDPEFKKVTPLIHDHMLDKKNAATLRL 1080
QY	1081 NHMKNKTSKKNEMVQOKKECPIPPOANDPMSFPKMLFLPESARWIORHGNLSLNSG 1140
DB	1081 NHMKNKTSKKNEMVQOKKECPIPPOANDPMSFPKMLFLPESARWIORHGNLSLNSG 1140
QY	1141 QGSPKOLVLSGPEKSEVQGNFLSEKKNVVGGEFTKDVGLKEKVPSSRNPLETNLDN 1200
DB	1141 QGSPKOLVLSGPEKSEVQGNFLSEKKNVVGGEFTKDVGLKEKVPSSRNPLETNLDN 1200

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OY 1201 LHEENTHNOEKKIOEIEKEKTELIOENVVLFOHTVTGTRKNFKKILFLSTRONVESSYD 1260
DB 1201 LHEENTHNOEKKIOEIEKEKTELIOENVVLFOHTVTGTRKNFKKILFLSTRONVESSYD 1260
OY 1261 GAYAPVLDPFRSLNDSTNRTKKTAFHFSKGOEBENLEGLONOTKOIWEKACTTRISPT 1320
DB 1261 GAYAPVLDPFRSLNDSTNRTKKTAFHFSKGOEBENLEGLONOTKOIWEKACTTRISPT 1320
OY 1321 SOONFVTOBSKRALKORPLPLEETELERKRIIVYDPTSTOWSKMKHLTPSTLLDIDYNEKE 1380
DB 1321 SOONFVTOBSKRALKORPLPLEETELERKRIIVYDPTSTOWSKMKHLTPSTLLDIDYNEKE 1380
OY 1381 KGAITOSPDLCLTRSHSTIPQANRSPPLIAYVSSPSTIRYITLRYLRODNSSHLPAASY 1440
DB 1381 KGAITOSPDLCLTRSHSTIPQANRSPPLIAYVSSPSTIRYITLRYLRODNSSHLPAASY 1440
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DB 1441 RKKDSGOESSHFLQAGKKNLSLAILTLEMTGDOREVGSLGTATNSVYTKKVENTVLP 1500
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DB 1501 KPDLPKTSGKVELLPKHVITQKOLPEETESNGSGHDLVEGSLQGTGAIKNWEANRP 1560
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DB 1561 GVPPLRATATSSAKTSPSKLDPDANDNHTGQIPKEEMKSOKESEKTAFAKKDTILSL 1620
OY 1621 NCESNHAIAAINEGOKPEIEVYTAOKGRTBLCSONPVYLKRHOREITRTTLOSDOE 1680
DB 1621 NCESNHAIAAINEGOKPEIEVYTAOKGRTBLCSONPVYLKRHOREITRTTLOSDOE 1680
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DB 1681 IDYDDTISEMKKEPDFIYDEENOSPRSFOKTRHFYIAAVERLDYDGMSSSPHVLNRP 1740
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DB 1741 AOGSGVPOFKKVVFOETDGSFTQPIYKSELNEHGLGEPYINAEVEDNIMTTPNQASR 1800
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OY 1861 DLEKDVHSGLIGPLVCHTNTLNPAGHROVYVOEFALFTIIFDEFSWTFENMERNCRA 1920
DB 1861 DLEKDVHSGLIGPLVCHTNTLNPAGHROVYVOEFALFTIIFDEFSWTFENMERNCRA 1920
OY 1921 PCNIOEDPTPKENYRHHAINGYIMDTLPGLVMAODORIRMYILLSGNSMENHSHIFSGH 1980
DB 1921 PCNIOEDPTPKENYRHHAINGYIMDTLPGLVMAODORIRMYILLSGNSMENHSHIFSGH 1980
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DB 2161 PPIIARYIRLAPHYRSTIRSLRMLGCOLNCSMPGLMESKASIDAOITASSYTTNFA 2220
OY 2221 TMSPSKARLHLOGRSNMRPOVNNPKEMWLDVDFOKTAKVGVGTQGVKSILTSMTYKBEFL 2280
DB 2221 TMSPSKARLHLOGRSNMRPOVNNPKEMWLDVDFOKTAKVGVGTQGVKSILTSMTYKBEFL 2280
OY 2281 ISSSODGHQWTLFQNGKVKVFOGNDSTPVPVNSIDPRLTLRLRIHQSWHQAIALRM 2340

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DB 2281 ISSSODGHQWTLFQNGKVKVFOGNDSTPVPVNSIDPRLTLRLRIHQSWHQAIALRM 2340
OY 2341 EVLGECAODLY 2351
DB 2341 EVLGECAODLY 2351

RESULT 15
AAW11362
ID AAW11362 standard; Protein; 2351 AA.
AC AAW11362;
X 18-NOV-1997 (first entry)
DT
XX
XX Active Factor VIII:C analogue L277X.
DE
XX Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW plasma protease; thrombin; immunogen; antibody; haemophilic therapy;
KW proteolytic cleavage.
OS Homo sapiens.
OS Synthetic.
XX
XX Key Location/Qualifiers
FH peptide 1..19
FT /note= "signal peptide"
FT Protein 20..2351
FT /note= "mature Factor VIII:C"
FT Region 20..1667
FT /note= "heavy chain fragment"
FT Modified-site 296
FT /label= Phe, Glu, Pro
FT Region 1668..2350
FT /note= "light chain fragment"
FT Domain 760..1667
FT /note= "B domain"

W09703195-A1.
30-JAN-1997.
09-JUL-1996; 96MO-US11444.
11-JUL-1995; 95US-0001025.
(CHIR ) CHIRON CORP.
Cohen FE, Hung DT, Innis M;
WPI; 1997-119050/11.

Factor VIII:C analog modified adjacent to a non-activating Arg
residue - used in the treatment of haemophilias, by improvement of
haemostasis
Claim 14; Page -: 90pp; English.

AAW1330-W11472 represent active Factor VIII:C analogues of the
invention. These sequences were created by mutating the wild type Factor
VIII:C coding sequence (see AAG51357) using mutagenic primers. The
analogues comprise a native Factor VIII:C polypeptide modified at a site
adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
dipeptide is created. Factor VIII:C is a large glycoprotein that
participates in the blood coagulation cascade that ultimately converts
soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
deficiency in Factor VIII:C is responsible for haemophilia A, which is an
X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
activated by plasma proteases, such as thrombin. During activation the
mature polypeptide is cleaved to generate heavy and light chain fragments
that are further cleaved. Complexes of two or more of the analogues,

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CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophilia, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.

XX Sequence 2351 AA:

Query Match 100.0%; Score 12413; DB 18; Length 2351;

Best Local Similarity 100.0%; Pred. No. 0;

Matches 2350; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 1 MOELSTCFCLRCFSATRRYYLGAVELSMQMSDGLPYDARPPVKKSPFN 60  
DB 1 MOELSTCFCLRCFSATRRYYLGAVELSMQMSDGLPYDARPPVKKSPFN 60  
QY 61 TSVYVKKTLPEYFDHLFNIAKPRPPMGLLGPITQAEVYDIYVITLKMASSHYSLHAY 120  
DB 61 TSVYVKKTLPEYFDHLFNIAKPRPPMGLLGPITQAEVYDIYVITLKMASSHYSLHAY 120  
QY 121 GVSYWKASGAEYDDOTSOREKEDKVPGGSHYVQVLKENGPMASDPLCLTYSLSH 180  
DB 121 GVSYWKASGAEYDDOTSOREKEDKVPGGSHYVQVLKENGPMASDPLCLTYSLSH 180  
QY 181 VDLVKDNLNSGLIGALVCREGSLAKEKTOTLHKFTLLFAVDEGKSMHSETKNSLMODRD 240  
DB 181 VDLVKDNLNSGLIGALVCREGSLAKEKTOTLHKFTLLFAVDEGKSMHSETKNSLMODRD 240  
QY 241 AASARAPKMHYVNGVYNSLPLGICHRKSVYHVMGTTEVHNSIFLGSHFTLYRNH 300  
DB 241 AASARAPKMHYVNGVYNSLPLGICHRKSVYHVMGTTEVHNSIFLGSHFTLYRNH 300  
QY 301 ROASLEISPTIFLTAOTLLMDLGOFLFCHSHSQHDMAYKVYDSCPEEPOLRMKNE 360  
DB 301 ROASLEISPTIFLTAOTLLMDLGOFLFCHSHSQHDMAYKVYDSCPEEPOLRMKNE 360  
QY 361 EAEDYDDDLTDESEMDVYRFDDNSPFSFIOIRSVAKKHPTKWYHIAAEEDMDVAPLYLA 420  
DB 361 EAEDYDDDLTDESEMDVYRFDDNSPFSFIOIRSVAKKHPTKWYHIAAEEDMDVAPLYLA 420  
QY 421 PDDBSYKSOYLNNGPOIRGKRYKRYPMAYTDEFKTRALIOHESITLGLLYGVOGDTL 480  
DB 421 PDDBSYKSOYLNNGPOIRGKRYKRYPMAYTDEFKTRALIOHESITLGLLYGVOGDTL 480  
QY 481 LIIFKNOASRPYNIYPHGITDVNPLYSRLRPKGVKHLKDEPILPGEIFKXKWTYVEDGP 540  
DB 481 LIIFKNOASRPYNIYPHGITDVNPLYSRLRPKGVKHLKDEPILPGEIFKXKWTYVEDGP 540  
QY 541 TKSDPRCLTRYSSSFVMMERDLASGLIPLLICRKESVDORGNOIMSDRNVILFVSFDE 600  
DB 541 TKSDPRCLTRYSSSFVMMERDLASGLIPLLICRKESVDORGNOIMSDRNVILFVSFDE 600  
QY 601 NRSWLTENIORPLPNAGVOLDEPFOASNTMSTINGVFSLOISYGLHVAWYTLIS 660  
DB 601 NRSWLTENIORPLPNAGVOLDEPFOASNTMSTINGVFSLOISYGLHVAWYTLIS 660  
QY 661 IGAOTDFLSVFFSGYTFKHKMYEDTLTLPFPGSETFVSMENPGLMTLLGCHNSDFNRNG 720  
DB 661 IGAOTDFLSVFFSGYTFKHKMYEDTLTLPFPGSETFVSMENPGLMTLLGCHNSDFNRNG 720  
QY 721 MTALLKVSCKDKNTGVDYEDYSIEDISAYLLSKNNAIEPRFSQNSNHPSTRKQKNATTI 780  
DB 721 MTALLKVSCKDKNTGVDYEDYSIEDISAYLLSKNNAIEPRFSQNSNHPSTRKQKNATTI 780  
QY 781 PENDIEKTDPMFAHRTPMKIQNVSSDMLMLRQSPTPHGLSLDLOEAKETFSDDPS 840  
DB 781 PENDIEKTDPMFAHRTPMKIQNVSSDMLMLRQSPTPHGLSLDLOEAKETFSDDPS 840  
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DB 841 PGALDSNNSLSEMTNHFHPOLHSGDMVFTPSSGQLRLNKLCTATATLKLKLDKVVST 900

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DB 1021 KTSNNSATNKRTHIDPSSLLENSPVSQNTLESDETFKKVTPPLIHDBMLDKNATLRL 1080  
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DB 1081 NMSKTKTSSKNEMVYQOKKEGPIPPDQNDNSFFKMLFLPESARWIOPTHGKNSLNSG 1140  
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DB 1321 SOONFVTOBKRALQKOPRLPLEETLEKRIIYDQTSQSKMKNLFTSTLOIDYNEKE 1380  
QY 1381 KCAITQSPSLDCITLRSHSIPQANSPLPIAKVSSPFSIRPIYLYTRVLFQDNSSHLPAAS 1440  
DB 1381 KCAITQSPSLDCITLRSHSIPQANSPLPIAKVSSPFSIRPIYLYTRVLFQDNSSHLPAAS 1440  
QY 1441 RKDQSGVOESSHFLQGAKKNNLSLAILTLEMTQDQREVCSLGSATNSVTYKKEVNTVLP 1500  
DB 1441 RKDQSGVOESSHFLQGAKKNNLSLAILTLEMTQDQREVCSLGSATNSVTYKKEVNTVLP 1500  
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DB 1621 NACESNHAIAINEGONKPEIEVYMAKOGRTERLCSQNPVLRKHQREITRTTLOSQDEE 1680  
QY 1681 IDYDQTTISVEKKEDDIYDEBENSPPSPFKKTRHYFLAAVERLMDVGMSSPHVYRNR 1740  
DB 1681 IDYDQTTISVEKKEDDIYDEBENSPPSPFKKTRHYFLAAVERLMDVGMSSPHVYRNR 1740  
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DB 1741 AOSGSVPQFKKVVYQEFITGSGTOPLVYGEINELGLGFTYIAEYEDNIWYTRRNQASR 1800  
QY 1801 PYSFYSLSIYEEDQOGAEPKKNVFNKNETKYTFWKVQHMAPTKDEDFCKAAYFSDV 1860  
DB 1801 PYSFYSLSIYEEDQOGAEPKKNVFNKNETKYTFWKVQHMAPTKDEDFCKAAYFSDV 1860  
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DB 1861 DLEKTVHSGLIGPLVCCHNTLNPAHAGVOYVQFALFTIDERTKSYFTENNERCKRA 1920  
QY 1921 PCNIQMEDPTFKENYFHAINGYIMDTLPGLVMAODORIMWYLLSGSNNENIHSIHSGH 1980  
DB 1921 PCNIQMEDPTFKENYFHAINGYIMDTLPGLVMAODORIMWYLLSGSNNENIHSIHSGH 1980

QY 1981 VFTVRKKEEYKMAIYNLYPGVEFYEMLPKAGIMPRVECLIGHHLHAGMSTLEFYYSNKC 2040  
DB 1981 VFTVRKKEEYKMAIYNLYPGVEFYEMLPKAGIMPRVECLIGHHLHAGMSTLEFYYSNKC 2040  
QY 2041 QTPPLGMSAGHTRDQITASGQGVQNAFKLARLHSGSINAMSTKEPPSWIKYDLAPMT 2100  
DB 2041 QTPPLGMSAGHTRDQITASGQGVQNAFKLARLHSGSINAMSTKEPPSWIKYDLAPMT 2100  
QY 2101 HGKIKTGAROKFSSLYISOFIIMYSLDGKKMOTRGANSTGTLWVFFGANDSSGKIHNFN 2160  
DB 2101 HGKIKTGAROKFSSLYISOFIIMYSLDGKKMOTRGANSTGTLWVFFGANDSSGKIHNFN 2160  
QY 2161 PPIIARIRLHPHYSTRSLRMEIIMGDLNSCMPLGMSKAIISAOTASSYFTNMEA 2220  
DB 2161 PPIIARIRLHPHYSTRSLRMEIIMGDLNSCMPLGMSKAIISAOTASSYFTNMEA 2220  
QY 2221 TWSPSKARLHOGKSNMARPQVNNPKEMLYQDFQKTKMYGVTTGQVKSLLTSMYKEFL 2280  
DB 2221 TWSPSKARLHOGKSNMARPQVNNPKEMLYQDFQKTKMYGVTTGQVKSLLTSMYKEFL 2280  
QY 2281 ISSSQDGHQWTLFPQNGKVKVFEQGNODSFTPVNSLDPELITRYLRIHQSWVHOIALRM 2340  
DB 2281 ISSSQDGHQWTLFPQNGKVKVFEQGNODSFTPVNSLDPELITRYLRIHQSWVHOIALRM 2340  
QY 2341 EYVLCGEADLY 2351  
DB 2341 EYVLCGEADLY 2351

RESULT 16  
AAP81113  
ID AAP81113 standard: protein: 2351 AA.  
XX AAP81113;  
XX 08-OCT-1990 (first entry)  
XX Factor VIII encoded by cDNA insert of pCLB89.  
XX Factor VIII; blood clotting disorders.  
XX Homo sapiens.  
XX Key Location/Qualifiers  
XX Peptide 1..19  
XX /label=signal sequence  
XX  
XX EP253455-A.  
XX 20-JAN-1988.  
XX 20-JUL-1987; 87EP-0201379.  
XX 18-JUL-1986; 86GB-0017594.  
XX 03-DEC-1986; 86GB-0030699.  
XX (KONN ) GIST-BROCADES NV.  
XX Van Ooyen AJJ, Andreoli PM, Van Mourik JA, Pannekoek H;  
XX WPI; 1988-015822/03.  
XX NPSDB: N81439.  
XX Expression system for producing factor VIII polypeptide in  
XX microbial cells - contg. open reading frame and functional  
XX initiation and termination regions.  
XX  
XX Disclosure: : 02pp; English.

CC is useful for treating blood clotting disorders.  
XX  
SQ Sequence 2351 AA:  
Query Match 100.0%; Score 12412; DB 9; Length 2351;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2350; Conservative 0; Mismatches 1; Indels 0; Gaps 0;  
QY 1 MOELSTCFEFLCLRFCSATRRYVGAVALSMOYSDGLSELPVDAAPPVPKSPFPN 60  
DB 1 MOELSTCFEFLCLRFCSATRRYVGAVALSMOYSDGLSELPVDAAPPVPKSPFPN 60  
QY 61 TSYVYKTLFEPFDHLEFNIAKRPPMGLLOPTIOAVYDVVYITLKMAHSPISLAV 120  
DB 61 TSYVYKTLFEPFDHLEFNIAKRPPMGLLOPTIOAVYDVVYITLKMAHSPISLAV 120  
QY 121 GVSVMKASGAEYDDQTSOREKEDDKVFPGSGSHYVMQVLEKNGPMASDPLCLVSYLSR 180  
DB 121 GVSVMKASGAEYDDQTSOREKEDDKVFPGSGSHYVMQVLEKNGPMASDPLCLVSYLSH 180  
QY 181 VDLVNDLNSGLIGALLVCRGSLAKKETOTLHKFTLFAVPDEGKSHSEPTKNSLMODRD 240  
DB 181 VDLVNDLNSGLIGALLVCRGSLAKKETOTLHKFTLFAVPDEGKSHSEPTKNSLMODRD 240  
QY 181 VDLVNDLNSGLIGALLVCRGSLAKKETOTLHKFTLFAVPDEGKSHSEPTKNSLMODRD 240  
DB 241 AASARAMPKMTVNGYVNSLPGLICHRKSVYWHVIGMTTPRVHSIFLEGHTELVRNH 300  
QY 241 AASARAMPKMTVNGYVNSLPGLICHRKSVYWHVIGMTTPRVHSIFLEGHTELVRNH 300  
DB 301 RQASLEISPTIFTLAQTLMDLGOFLIFCHISSHODMEAYVYVDSCEPEPOLMKKNE 360  
QY 301 RQASLEISPTIFTLAQTLMDLGOFLIFCHISSHODMEAYVYVDSCEPEPOLMKKNE 360  
QY 361 EAEDYDDDLTSEMDVYRFPDDNSPSFQIRSVAKKPKTMVHYIAAEEDMDYAPVLA 420  
DB 361 EAEDYDDDLTSEMDVYRFPDDNSPSFQIRSVAKKPKTMVHYIAAEEDMDYAPVLA 420  
QY 421 PDORSTKQYLNNGPQIRGKRYKVFMAVYDEFEKTRREALOHSGLLPVLYGEVGTLL 480  
DB 421 PDORSTKQYLNNGPQIRGKRYKVFMAVYDEFEKTRREALOHSGLLPVLYGEVGTLL 480  
QY 481 LIIFKQASRPYNIYPGITDVAPRLYSRRLPKGVNHLKDFPILGELIFKXKWTYVEDGP 540  
DB 481 LIIFKQASRPYNIYPGITDVAPRLYSRRLPKGVNHLKDFPILGELIFKXKWTYVEDGP 540  
QY 541 TKSDDPCLTRYYSFVMMERDLASGILGPLLCTYESVDONGNINSDRNYILFSVDE 600  
DB 541 TKSDDPCLTRYYSFVMMERDLASGILGPLLCTYESVDONGNINSDRNYILFSVDE 600  
QY 541 TKSDDPCLTRYYSFVMMERDLASGILGPLLCTYESVDONGNINSDRNYILFSVDE 600  
DB 601 NNSWYLTENIQRLPNPAGVQLEDPFQASNTMHSINGYVDSIQLSVCLHEVAYWYLS 660  
QY 601 NNSWYLTENIQRLPNPAGVQLEDPFQASNTMHSINGYVDSIQLSVCLHEVAYWYLS 660  
DB 601 NNSWYLTENIQRLPNPAGVQLEDPFQASNTMHSINGYVDSIQLSVCLHEVAYWYLS 660  
QY 661 IGAQTDFLSVFSGYTFKHKMYVEDTLTLPFPGSGETVMSMENGLMILGCHNSDFRRNG 720  
DB 661 IGAQTDFLSVFSGYTFKHKMYVEDTLTLPFPGSGETVMSMENGLMILGCHNSDFRRNG 720  
QY 721 MTRALKVSSCDKNKGVDYEDSYEDISAVYLSNNAIIPERSQNSRHPRSRQKRNATTI 780  
DB 721 MTRALKVSSCDKNKGVDYEDSYEDISAVYLSNNAIIPERSQNSRHPRSRQKRNATTI 780  
QY 781 PENDIEKTDPMFAHRTMPKIQNVSSDILLMLKROSPPHGLSLSDIQEAKYETSDPS 840  
DB 781 PENDIEKTDPMFAHRTMPKIQNVSSDILLMLKROSPPHGLSLSDIQEAKYETSDPS 840  
QY 841 PGALISNNSISEMTHFRPOLHSGDWVFPESGQDLRLNEKLTGTATATLKLDPKVSST 900  
DB 841 PGALISNNSISEMTHFRPOLHSGDWVFPESGQDLRLNEKLTGTATATLKLDPKVSST 900  
QY 901 SNMLSTIPSDNLAAGDNTSSIGSPSMVYHDSQLODTLFGKKSPTRESGPISLEE 960  
DB 901 SNMLSTIPSDNLAAGDNTSSIGSPSMVYHDSQLODTLFGKKSPTRESGPISLEE 960  
QY 961 NNDSKLLESGLMNSQESSMCKNVYSTSGRLFKGRAGHAPALLTKONALEKVISILKTN 1020



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Db      961  NNDKSLLEGLMNSOESSWKNNSTFSGRLKGRRAHPALITKDNALTKVSLILKTN 1020
Qy      1021 KTSNNSATNRKTHIDGSPLLIENSPYMONILESDTEERKKTPLIHDMMDKNATRLR 1080
Db      1021 KTSNNSATNRKTHIDGSPLLIENSPYMONILESDTEERKKTPLIHDMMDKNATRLR 1080
Qy      1081 NMSNKTSSKMEVQOKKEGPIDPAONPDMSFFKMLFPEASARWIOPTHGKNSLNSG 1140
Db      1081 NMSNKTSSKMEVQOKKEGPIDPAONPDMSFFKMLFPEASARWIOPTHGKNSLNSG 1140
Qy      1141 QGSPKQVSLCPREKSVGQNFLEKAKVYVGGFETKVGJLKEWPESSRNLFPTMDX 1200
Db      1141 QGSPKQVSLCPREKSVGQNFLEKAKVYVGGFETKVGJLKEWPESSRNLFPTMDX 1200
Qy      1201 LHEHNTNHOEKKIOEIEKEKELLIOENVVLPOIHTVTGKNPMKMLFLLSTRONVEGSSYD 1260
Db      1201 LHEHNTNHOEKKIOEIEKEKELLIOENVVLPOIHTVTGKNPMKMLFLLSTRONVEGSSYD 1260
Qy      1261 GATAPVLODPRSLNSTNRKTHAHSKKGEBENLEGLNQTQIVKACTRISPT 1320
Db      1261 GATAPVLODPRSLNSTNRKTHAHSKKGEBENLEGLNQTQIVKACTRISPT 1320
Qy      1321 SQONFVYQSRKALQKQFLPLEETELEKRIIVDTSTOMSKNKHLPSTLTQIDYNEKE 1380
Db      1321 SQONFVYQSRKALQKQFLPLEETELEKRIIVDTSTOMSKNKHLPSTLTQIDYNEKE 1380
Qy      1381 KGATOSPISDCLTRSHSPQANRSPPLIAKVSFSPISPIRYLTLYLVLFQDNSSHLPAASY 1440
Db      1381 KGATOSPISDCLTRSHSPQANRSPPLIAKVSFSPISPIRYLTLYLVLFQDNSSHLPAASY 1440
Qy      1441 RKKDSGVQESSHFLQKAKNNLSLAILLEMTGQORVGSGLSTANSYTKYKENVYLP 1500
Db      1441 RKKDSGVQESSHFLQKAKNNLSLAILLEMTGQORVGSGLSTANSYTKYKENVYLP 1500
Qy      1501 KPDLPTSGVVELLPVHTIYQKDLFPTETNSGSPGHLIDVSGSLQGTGALIKMEANRP 1560
Db      1501 KPDLPTSGVVELLPVHTIYQKDLFPTETNSGSPGHLIDVSGSLQGTGALIKMEANRP 1560
Qy      1561 KVPFLKVAATESNAKTPSKLIDPLAMDHYGTOIPKEEMKSQKSEKTAFFKKTTIISL 1620
Db      1561 KVPFLKVAATESNAKTPSKLIDPLAMDHYGTOIPKEEMKSQKSEKTAFFKKTTIISL 1620
Qy      1621 NACESNHAIAINEGONKEIEVTWAKOGRTERLCSNPVPLKRHOIREITRTTLOSDEE 1680
Db      1621 NACESNHAIAINEGONKEIEVTWAKOGRTERLCSNPVPLKRHOIREITRTTLOSDEE 1680
Qy      1681 IDYDQTSVEMKEDDIDEDENOSPRSPOKKTIRHYFIAVERLMDYGMSSSPHYLNR 1740
Db      1681 IDYDQTSVEMKEDDIDEDENOSPRSPOKKTIRHYFIAVERLMDYGMSSSPHYLNR 1740
Qy      1741 AOSGSVPQFKKVVFOETDGSFTOPLYRGEINLGLGPYIRAEVDNIMVTFRNQSAR 1800
Db      1741 AOSGSVPQFKKVVFOETDGSFTOPLYRGEINLGLGPYIRAEVDNIMVTFRNQSAR 1800
Qy      1801 PYSFYSLSIYEEOOROGAEPKRNFKYKNETKYFWKVOHHMAPTKDEDFCKAMAYFSDV 1860
Db      1801 PYSFYSLSIYEEOOROGAEPKRNFKYKNETKYFWKVOHHMAPTKDEDFCKAMAYFSDV 1860
Qy      1861 DLEKDVHSGILGPLVCHTILNPAHGRQVYQEEALFETLIDETNSWYTEMENKRA 1920
Db      1861 DLEKDVHSGILGPLVCHTILNPAHGRQVYQEEALFETLIDETNSWYTEMENKRA 1920
Qy      1921 PCNIOMEDPTFKENYRHAINGYIMDTLPGLVMAODQIRMYLLSLMGSNENIHSIFSCH 1980
Db      1921 PCNIOMEDPTFKENYRHAINGYIMDTLPGLVMAODQIRMYLLSLMGSNENIHSIFSCH 1980
Qy      1981 VFTVRKKEEYKMALYNLYPCVFETVMDPSKAGIRVCLIGELHAGMSTLFLVYSKNC 2040
Db      1981 VFTVRKKEEYKMALYNLYPCVFETVMDPSKAGIRVCLIGELHAGMSTLFLVYSKNC 2040
Qy      2041 QTPIGMASGHIRDFQITASGOYQOMAPKLARLHYSGINASTKEPFSWKVLLAPMI 2100

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Db      2041 QTPIGMASGHIRDFQITASGOYQOMAPKLARLHYSGINASTKEPFSWKVLLAPMI 2100
Qy      2101 HGITQGARQKFSLSYISOFIIMYSLDCKKMQYRNGNSTGLTWFFGNVDSGIRKHNIFN 2160
Db      2101 HGITQGARQKFSLSYISOFIIMYSLDCKKMQYRNGNSTGLTWFFGNVDSGIRKHNIFN 2160
Qy      2161 PPIIARTIRLHPHYSTRSTLAMELNGDLSGSMPLGMSKASIPDAQITASSYPTNMEA 2220
Db      2161 PPIIARTIRLHPHYSTRSTLAMELNGDLSGSMPLGMSKASIPDAQITASSYPTNMEA 2220
Qy      2221 TWSPSKARLHLOGKSNAMRPQVNNPKEMLOVDFQKTKMVTGTTQGVKSLISMYKEFL 2280
Db      2221 TWSPSKARLHLOGKSNAMRPQVNNPKEMLOVDFQKTKMVTGTTQGVKSLISMYKEFL 2280
Qy      2281 ISSQDGHQWTLFPQNGKXKVPQGNODSFTPVNSLDPPLITRYLRIRHPQSWHOIALRM 2340
Db      2281 ISSQDGHQWTLFPQNGKXKVPQGNODSFTPVNSLDPPLITRYLRIRHPQSWHOIALRM 2340
Qy      2341 EVLGEAODLY 2351
Db      2341 EVLGEAODLY 2351

RESULT 17
AAP80659
ID AAP80659 standard: protein; 2351 AA.
AC AAP80659;
DF 29-OCT-1990 (first entry)
DE Sequence of human Factor VIII signal sequence and mature protein
  encoded on plasmid pCLB89.
KW Haemophilia A; bloodclotting; treatment; diagnosis.
OS Homo sapiens.
FH Key Location/Qualifiers
FT Peptide 1..19
FT /note="signal peptide"
FT Protein 20..2351
PN EP294910-A.
PD 14-DEC-1988.
PF 13-JUN-1988; 88EP-0201209.
PR 12-JUN-1987; 87EP-0201121.
PA (KONN ) GIST-BROCADES NV.
PI van Ooyen AJJ, Pannekoek H, Verbeet MP, van Leen RW;
DR WPI; 1988-355361/50.
DR N-PSDB; AANB1096.
PT Proteins having Factor VIII activity -
PT comprising deletion mutant proteins of Factor VIII in which
PT central region has been deleted
PS Example; Fig 1; 37pp; English.
CC The isolation of Factor VIII mRNA from human liver, and the preparation,
CC purification and identification of its cDNA and its assembly in
CC pEPI21 resulting in plasmid pCLB89 have been described in patent
CC application EP 0253455. The Factor VIII polypeptides of the invention
CC include deletion mutant proteins of Factor VIII in which all of central
CC region or "B domain" as well as a portion of the 92 kd region has been
CC deleted. The polypeptides have enhanced Factor VIII activity and/or
CC decreased immunogenicity and can be used for the treatment of
CC Haemophilia A. They can also be used to prepare antibodies. The Abs.

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CC can be used to determine the concn. of Factor VIII in a body fluid.

XX Sequence 2351 AA;

Query Match 100.0%; Score 12412; DB 9; Length 2351;

Best Local Similarity 100.0%; Pred. No. 0;

Matches 2350; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

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OY 1 MQLSTCFELCLRFCEFSATRRYTGAVELSMQSDGLGELPVDPARPPRPKSPFN 60
DB 1 MQLSTCFELCLRFCEFSATRRYTGAVELSMQSDGLGELPVDPARPPRPKSPFN 60
OY 61 TSVYKKTLEFPEFDHLFNIAKPRPPMGLGPTIOAEYDVIYITLKMASSHPVSLHAY 120
DB 61 TSVYKKTLEFPEFDHLFNIAKPRPPMGLGPTIOAEYDVIYITLKMASSHPVSLHAY 120
OY 121 GSVYKASEGAEYDDQTSQREKEDDKVPFGSHYVQVLEKENGPMASDPLCLTYSLSH 180
DB 121 GSVYKASEGAEYDDQTSQREKEDDKVPFGSHYVQVLEKENGPMASDPLCLTYSLSH 180
OY 181 VDLVLDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDGKSMHSETKNSLMQDRD 240
DB 181 VDLVLDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDGKSMHSETKNSLMQDRD 240
OY 241 AASARAMPKMTYNGVYNSLPGILGCHRSYVNHVIGMGTPEVHSLFLBQHTFLVRNH 300
DB 241 AASARAMPKMTYNGVYNSLPGILGCHRSYVNHVIGMGTPEVHSLFLBQHTFLVRNH 300
OY 301 ROASLEISPTFELTAQTLMDLQGFLLGCHISSHQHDGMEAYKVDSCPEPQRLMKNE 360
DB 301 ROASLEISPTFELTAQTLMDLQGFLLGCHISSHQHDGMEAYKVDSCPEPQRLMKNE 360
OY 361 EAEDYDDLTDSEMDVVRFPDDNSPSFTQIRSAVKKHPKTHVYIAEEEDMDYAPLVLA 420
DB 361 EAEDYDDLTDSEMDVVRFPDDNSPSFTQIRSAVKKHPKTHVYIAEEEDMDYAPLVLA 420
OY 421 PDRSRYKSOYLNNGPORIGRKYKVFMAATYDEFKTRERAIQHESSILGELLGEGVDTL 480
DB 421 PDRSRYKSOYLNNGPORIGRKYKVFMAATYDEFKTRERAIQHESSILGELLGEGVDTL 480
OY 481 LIIFKNQASRPYNTYPIGTDVDRPLXSRLLKGYKHLKOPPIPGELFKYKTYVYEDGP 540
DB 481 LIIFKNQASRPYNTYPIGTDVDRPLXSRLLKGYKHLKOPPIPGELFKYKTYVYEDGP 540
OY 541 TKSDBRCLTRYYSFVNMERDLASGLIGPLLICYESVDORGNOIMSDKRNVLFSVDE 600
DB 541 TKSDBRCLTRYYSFVNMERDLASGLIGPLLICYESVDORGNOIMSDKRNVLFSVDE 600
OY 601 NRSWYLTENIQRFLLPNPAGVLEDEPFOASNMISNGYVFDLSQVCLHEVAATWYLS 660
DB 601 NRSWYLTENIQRFLLPNPAGVLEDEPFOASNMISNGYVFDLSQVCLHEVAATWYLS 660
OY 661 IGAOTDFLSVFGSYTRKHKMYEDTLTLPFSGEYVPMEMERGLMIGCHNSDFRRG 720
DB 661 IGAOTDFLSVFGSYTRKHKMYEDTLTLPFSGEYVPMEMERGLMIGCHNSDFRRG 720
OY 721 MTALLKVSCKKNTGDIYEDYEDISAYLLSKNNAIEPRSFSONSRHSTROKOFNATY 780
DB 721 MTALLKVSCKKNTGDIYEDYEDISAYLLSKNNAIEPRSFSONSRHSTROKOFNATY 780
OY 781 PENDIKTDPMFAHRTMPKIQNVSSSDMLMLKQSPTPAGLSISDLQAKKETFSDPS 840
DB 781 PENDIKTDPMFAHRTMPKIQNVSSSDMLMLKQSPTPAGLSISDLQAKKETFSDPS 840
OY 841 PGALDSNNSLSSEMTHFPPQLHSGDMVFTPRESGQLRLNKLCTTAATLTKLDPKVSST 900
DB 841 PGALDSNNSLSSEMTHFPPQLHSGDMVFTPRESGQLRLNKLCTTAATLTKLDPKVSST 900
OY 901 SNNLSTIPSDNLAAGDNTSSLGPPSNPVHYDSQDLDTTLFGKSSPLTESGGLSISEE 960
DB 901 SNNLSTIPSDNLAAGDNTSSLGPPSNPVHYDSQDLDTTLFGKSSPLTESGGLSISEE 960
OY 961 NNDSKLLESGLMNSQESSMGKNVSTYESGRLFKGRRAHGPAALLTKDNALFKVYSILKTN 1020
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DB 961 NNDSKLLESGLMNSQESSMGKNVSTYESGRLFKGRRAHGPAALLTKDNALFKVYSILKTN 1020
OY 1021 KTSNKSATNRKTHIDPSSLIEBNSPVQNLISDTEFFKVTPLIHDBMLDKNATALRL 1080
DB 1021 KTSNKSATNRKTHIDPSSLIEBNSPVQNLISDTEFFKVTPLIHDBMLDKNATALRL 1080
OY 1081 NMSNKTSSKNMEMYQAKKEGPILPPQANPDNSFFKMLFLPESARNTQORTHGKNSLNSG 1140
DB 1081 NMSNKTSSKNMEMYQAKKEGPILPPQANPDNSFFKMLFLPESARNTQORTHGKNSLNSG 1140
OY 1141 OGSPKQULVSLGPEKVBEGONFLSKKKVYVGGFETTKVYGKLEKVFSSNKLFLTNLDN 1200
DB 1141 OGSPKQULVSLGPEKVBEGONFLSKKKVYVGGFETTKVYGKLEKVFSSNKLFLTNLDN 1200
OY 1201 LHENNTHNOBKKTQEBIEKKETLLQDENVVLPOIHTVYTGTRKMKNLFLSTROYNEGYD 1260
DB 1201 LHENNTHNOBKKTQEBIEKKETLLQDENVVLPOIHTVYTGTRKMKNLFLSTROYNEGYD 1260
OY 1261 GAYAPVLQDFRSLNDSTNRKKTTHAFSKGEEBNEGLGNQTKOIVKCYACTRISPT 1320
DB 1261 GAYAPVLQDFRSLNDSTNRKKTTHAFSKGEEBNEGLGNQTKOIVKCYACTRISPT 1320
OY 1321 SQONFVTOBRSKRALQOFRLPEFTELEKRIIVDDTQTSKMMKHLFPTLTQIDVNEKE 1380
DB 1321 SQONFVTOBRSKRALQOFRLPEFTELEKRIIVDDTQTSKMMKHLFPTLTQIDVNEKE 1380
OY 1381 KGAITOSPFLSDCLTRSHSTPOANRSPRLIAVSSFFSIRPYTLRVLFQDNSSHLPAAS 1440
DB 1381 KGAITOSPFLSDCLTRSHSTPOANRSPRLIAVSSFFSIRPYTLRVLFQDNSSHLPAAS 1440
OY 1441 RKDQSGVOESSHFLQAKKNNLSIALTLTLEMTGDQREVSIGTSATNSVYKKEVNTVLP 1500
DB 1441 RKDQSGVOESSHFLQAKKNNLSIALTLTLEMTGDQREVSIGTSATNSVYKKEVNTVLP 1500
OY 1501 KPDLPTKSGAVELLPPVHTYQKDLPEFTSGSPGHLDLVESSLQTEGAIKKNKANR 1560
DB 1501 KPDLPTKSGAVELLPPVHTYQKDLPEFTSGSPGHLDLVESSLQTEGAIKKNKANR 1560
OY 1561 GKVPFLVATNESSAKTPSKLDPRLAMDNHGTQTPKEBKSOEKSPETAKKODTLLS 1620
DB 1561 GKVPFLVATNESSAKTPSKLDPRLAMDNHGTQTPKEBKSOEKSPETAKKODTLLS 1620
OY 1621 NACESNHAIAINEGONKPEIEVTAQOGRTERLCSQNPVLRKHQREITRTTLQSDQEE 1680
DB 1621 NACESNHAIAINEGONKPEIEVTAQOGRTERLCSQNPVLRKHQREITRTTLQSDQEE 1680
OY 1681 IDYDPTISVEKKEDPDYDEDENSPSPQKTRHYFLAVERLMDYGMSSPHVLRNR 1740
DB 1681 IDYDPTISVEKKEDPDYDEDENSPSPQKTRHYFLAVERLMDYGMSSPHVLRNR 1740
OY 1741 AOSGVSQPFKKVYVQFETDGSFTQULYNGELNHLGILGPRYIRAEVEDNINVTFRQNASR 1800
DB 1741 AOSGVSQPFKKVYVQFETDGSFTQULYNGELNHLGILGPRYIRAEVEDNINVTFRQNASR 1800
OY 1801 PYSFYSLSLISEEDQOGAEPRKNFVKNEFKTYFVKVQHHMAPTKDEFOCKAMAFSDV 1860
DB 1801 PYSFYSLSLISEEDQOGAEPRKNFVKNEFKTYFVKVQHHMAPTKDEFOCKAMAFSDV 1860
OY 1861 DLEKDVHSGILGPLLCAHTNLTNPAGHGOVYVQEFALFTIIDEKTSKYFTENNERNCRA 1920
DB 1861 DLEKDVHSGILGPLLCAHTNLTNPAGHGOVYVQEFALFTIIDEKTSKYFTENNERNCRA 1920
OY 1921 PCNIDMEPPFKENYRFAHINQIMDTLPGLYMAQODRIRWLLMSGNSNEMIHSHFSGH 1980
DB 1921 PCNIDMEPPFKENYRFAHINQIMDTLPGLYMAQODRIRWLLMSGNSNEMIHSHFSGH 1980
OY 1981 VETVAKKEEYKMAALYULYGVGEVYEMLPKSAAGIMWRECLIEBHHAAMSTYFLVYSNKC 2040
DB 1981 VETVAKKEEYKMAALYULYGVGEVYEMLPKSAAGIMWRECLIEBHHAAMSTYFLVYSNKC 2040
OY 2041 QPILGMASGHIRDFQITAGGQYQGMAPLARIATHSGINAMSTKPEFSMIKVDLAPMII 2100
```

DB 2041 QTPLGASGHIRDFQITASGOYGOMAPKLARLHSGSINAMSTKEPFWIKVDLLAPMII 2100  
QY 2101 HGKGTQAROKFSSLYISQFIIMYSIDGKKMQYRGSTSTGLWVPFGNDSSGIRKHINFN 2160  
DB 2101 HGKGTQAROKFSSLYISQFIIMYSIDGKKMQYRGSTSTGLWVPFGNDSSGIRKHINFN 2160  
QY 2161 PPIIARIRLAPHYSTRITBELMGDLNCSMPLEGSKAISDAQITASSFTWFA 2220  
DB 2161 PPIIARIRLAPHYSTRITBELMGDLNCSMPLEGSKAISDAQITASSFTWFA 2220  
QY 2221 TWSPSKARLHOGSRNAMPQVNNPEKWLQVDFQKTKKVTGVTQGVSSLLTSMYKEFL 2280  
DB 2221 TWSPSKARLHOGSRNAMPQVNNPEKWLQVDFQKTKKVTGVTQGVSSLLTSMYKEFL 2280  
QY 2281 ISSQDGHQMTLFPQNGKVKVFQGNDSFTPVNSLDPPLITRYLRIRHPQSWHQAIALRM 2340  
DB 2281 ISSQDGHQMTLFPQNGKVKVFQGNDSFTPVNSLDPPLITRYLRIRHPQSWHQAIALRM 2340  
QY 2341 EVLGEAODLY 2351  
DB 2341 EVLGEAODLY 2351  
RESULT 18  
AAM11437 standard; Protein: 2351 AA.  
AAM11437:  
AC 20-NOV-1997 (first entry)  
DE Active Factor VIII:C analogue, delta 1644, + Pro insertion.  
XX  
XX AAM11437:  
XX  
XX 20-NOV-1997 (first entry)  
XX  
XX Active Factor VIII:C analogue, delta 1644, + Pro insertion.  
XX  
XX Factor VIII:C analogue; glycoprotein; blood coagulation cascade;  
KM fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KM plasma protease; thrombin; immunogen; antibody; haemophilia; therapy;  
KM proteolytic cleavage.  
XX  
XX Homo sapiens.  
OS Synthetic.  
XX  
XX Key  
FH 1..19 Location/Qualifiers  
FT Peptide  
FT /note= "signal peptide"  
FT Protein  
FT /note= "20..2351"  
FT Region  
FT /note= "mature Factor VIII:C"  
FT 20..1667  
FT /note= "heavy chain fragment"  
FT Misc-difference 1662..1663  
FT /note= "site of 1 residue deletion"  
FT Modified-site  
FT 1663  
FT /note= "inserted residue"  
FT Region  
FT 1668..2350  
FT /note= "light chain fragment"  
FT 760..1667  
FT Domain  
FT /note= "B domain"  
XX  
XX WO9703195-A1.  
XX  
XX 30-JAN-1997.  
XX  
XX 09-JUL-1996; 96WO-US11444.  
XX  
XX 11-JUL-1995; 95US-0001025.  
XX  
XX (CHIR ) CHIRON CORP.  
XX  
XX Cohen FE, Hung DT, Innis M;  
XX WPI; 1997-119050/11.  
XX  
XX Factor VIII:C analog modified adjacent to a non-activating Arg  
XX residue - used in the treatment of haemophiliacs. By improvement of

PT haemostasis  
XX  
PS Claim 31; Page -: 90pp; English.  
XX  
CC AAM11330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophiliacs, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX  
XX Sequence 2351 AA:  
SQ  
Query Match 100.0%; Score 12412; DB 18; Length 2351;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2350; Conservative 0; Mismatches 1; Indels 0; Gaps 0;  
QY 1 MOILSTCFCLLRPCSATRRYYLGAVELSMDYQSDGLBELVDARPPRPVKSFPFN 60  
DB 1 MOILSTCFCLLRPCSATRRYYLGAVELSMDYQSDGLBELVDARPPRPVKSFPFN 60  
QY 61 TSVYKKTLFEFTLHFNIAKPPPMGMLGPTQAEYDVTYITLKNASHPVSLNAV 120  
DB 61 TSVYKKTLFEFTLHFNIAKPPPMGMLGPTQAEYDVTYITLKNASHPVSLNAV 120  
QY 121 GVSYWKASGEAEYDQTSOREKEDKVFPGSHTYVWOLKENGPMASDPLCTYSYLSH 180  
DB 121 GVSYWKASGEAEYDQTSOREKEDKVFPGSHTYVWOLKENGPMASDPLCTYSYLSH 180  
QY 181 VDIYKDNISGLALNCRGSLAKKKTOTLKFLLFAVDECKSMHSTKSLMORPD 240  
DB 181 VDIYKDNISGLALNCRGSLAKKKTOTLKFLLFAVDECKSMHSTKSLMORPD 240  
QY 241 AASARAMPKMTVNGVYVNRSLPGLIGCHRSYVMHYTGMTPEVHSIFLEGTEPLVNRH 300  
DB 241 AASARAMPKMTVNGVYVNRSLPGLIGCHRSYVMHYTGMTPEVHSIFLEGTEPLVNRH 300  
QY 301 ROASLEISPTFLTAQTLMDLQGFLLCHISSHODMEAVYVVDSCPEEPOLRMKNNE 360  
DB 301 ROASLEISPTFLTAQTLMDLQGFLLCHISSHODMEAVYVVDSCPEEPOLRMKNNE 360  
QY 361 EAEDYDDDLTDEMDVYVFPDDNSPSTIOTRSYAKKHKTWVHVIAAEEDMDVYPIVIA 420  
DB 361 EAEDYDDDLTDEMDVYVFPDDNSPSTIOTRSYAKKHKTWVHVIAAEEDMDVYPIVIA 420  
QY 421 PDDRSYSQYLNNGPQRIGRKYYKVRPMAYTDETKYEDAIQHSGLIGPLLYGEVDTL 480  
DB 421 PDDRSYSQYLNNGPQRIGRKYYKVRPMAYTDETKYEDAIQHSGLIGPLLYGEVDTL 480  
QY 481 LIIFKNQASRPYNIYPHIGITDVPRLYSRRLPGVNHLDKDFILGELIFKYYKWTVEDGP 540  
DB 481 LIIFKNQASRPYNIYPHIGITDVPRLYSRRLPGVNHLDKDFILGELIFKYYKWTVEDGP 540  
QY 541 TKSPRCITRRYSSPVNNERDLASGLIGPLLCYESVDQNGNIMSDKRNLYLSVDE 600  
DB 541 TKSPRCITRRYSSPVNNERDLASGLIGPLLCYESVDQNGNIMSDKRNLYLSVDE 600  
QY 601 NRSWYLTENIQRLFPNPGVQLEDPFQASNMHSINQYVDSIQSLCYLHAYWYLLS 660  
DB 601 NRSWYLTENIQRLFPNPGVQLEDPFQASNMHSINQYVDSIQSLCYLHAYWYLLS 660

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Db      601 NRSWTLENIQRIPLPNAGVQLEDPPEQASINMHSINGYVFDLSIQVCLHEVAYWILS 660
Oy      661 IGAQTDFLSVFSGYTEFKRMVYEDTLTLPPSGEYEVMSMENPGLMLGCHNSDFNRG 720
Db      661 IGAQTDFLSVFSGYTEFKRMVYEDTLTLPPSGEYEVMSMENPGLMLGCHNSDFNRG 720
Oy      721 MTKALKVSSCDKNTGDVYEDSYEDIISAYLLSKNNAIEPRSFSONSHPTROKOFNATTI 780
Db      721 MTKALKVSSCDKNTGDVYEDSYEDIISAYLLSKNNAIEPRSFSONSHPTROKOFNATTI 780
Oy      781 PENDEKTDPEFAHRTMFKIQNVSSDQLMLLQSPTRPGLSLSDQPAKYTFSDPS 840
Db      781 PENDEKTDPEFAHRTMFKIQNVSSDQLMLLQSPTRPGLSLSDQPAKYTFSDPS 840
Oy      841 PGALDSNNSLSEMTNFRPOLHNSGDMVTPESGLOLRNLKLTQTAATELKKLFKVSST 900
Db      841 PGALDSNNSLSEMTNFRPOLHNSGDMVTPESGLOLRNLKLTQTAATELKKLFKVSST 900
Oy      901 SNNLISTIPSDNLAAGDNTSSSLGPPSMVHYDSQDLYTLFGKSSPLTESGGLSSEE 960
Db      901 SNNLISTIPSDNLAAGDNTSSSLGPPSMVHYDSQDLYTLFGKSSPLTESGGLSSEE 960
Oy      961 NNDKLTSSGLMNSOESSMGKNVSSREGRLFKGRRAHGALLTKNALFKYSTILKTN 1020
Db      961 NNDKLTSSGLMNSOESSMGKNVSSREGRLFKGRRAHGALLTKNALFKYSTILKTN 1020
Oy      1021 KTSNNSATNRKTHIDGSLIENSPSWONILESDFEKKVYPLIDRMLMDKNATRL 1080
Db      1021 KTSNNSATNRKTHIDGSLIENSPSWONILESDFEKKVYPLIDRMLMDKNATRL 1080
Oy      1081 NMSNKTYSKKNMEMVOQKKEGPIPDQNPDMFSFKMLFLPESARWIDORTGKNSLNG 1140
Db      1081 NMSNKTYSKKNMEMVOQKKEGPIPDQNPDMFSFKMLFLPESARWIDORTGKNSLNG 1140
Oy      1141 OGSPKQOLVSLGPEKSVESGONFLSEKNKYVVGKEFTKDGLEKEMFPSSRLPLTNDN 1200
Db      1141 OGSPKQOLVSLGPEKSVESGONFLSEKNKYVVGKEFTKDGLEKEMFPSSRLPLTNDN 1200
Oy      1201 LHEBNTHQEKKIOEIELEKKEKTLIDENYVLPQIHVYGTGNFKNPLFLSTQONEGSYD 1260
Db      1201 LHEBNTHQEKKIOEIELEKKEKTLIDENYVLPQIHVYGTGNFKNPLFLSTQONEGSYD 1260
Oy      1261 GAVAPVLODFRSLNDSTNRKTKHTAHFSKGEENLEGLNQTKQIYEKYACTRISPT 1320
Db      1261 GAVAPVLODFRSLNDSTNRKTKHTAHFSKGEENLEGLNQTKQIYEKYACTRISPT 1320
Oy      1321 SQONFVQSRKRALKOPRLPLETLEKRIIYDPTSTOWSKNNKHLPTSTLOIDYNKE 1380
Db      1321 SQONFVQSRKRALKOPRLPLETLEKRIIYDPTSTOWSKNNKHLPTSTLOIDYNKE 1380
Oy      1381 KGAIOSPLSDCLTRSHSTIQANRSPPLAKYSSPSPRIYLTRVLFDONSHLPAASY 1440
Db      1381 KGAIOSPLSDCLTRSHSTIQANRSPPLAKYSSPSPRIYLTRVLFDONSHLPAASY 1440
Oy      1441 RKKDSGVDESSHFLQGAKKNNLSLALILEMTGDQREVSLGTSAVNSVYKKEVNTLP 1500
Db      1441 RKKDSGVDESSHFLQGAKKNNLSLALILEMTGDQREVSLGTSAVNSVYKKEVNTLP 1500
Oy      1501 KPDLPTSGKYELLPKVHIYQKDLFPTETSNGSPCHLDIVEGSLGCTGALKMWEARP 1560
Db      1501 KPDLPTSGKYELLPKVHIYQKDLFPTETSNGSPCHLDIVEGSLGCTGALKMWEARP 1560
Oy      1561 GAVPPLVATSSAKTSPSKLLDPLANDNHYGQIPKEKMSQEKSPKTAFFKKTJLIL 1620
Db      1561 GAVPPLVATSSAKTSPSKLLDPLANDNHYGQIPKEKMSQEKSPKTAFFKKTJLIL 1620
Oy      1621 NACESNHAIAAINGOKMPEIEVYMAKOGRETRLCSONPVLKRHORREITRTTLOSDEE 1680
Db      1621 NACESNHAIAAINGOKMPEIEVYMAKOGRETRLCSONPVLKRHORREITRTTLOSDEE 1680
Oy      1681 IDYDPTISYEKKEDPDIYDEENOSPRSFQKTRHNFIAVARELDYDMSSPVLNRR 1740
Db      1681 IDYDPTISYEKKEDPDIYDEENOSPRSFQKTRHNFIAVARELDYDMSSPVLNRR 1740

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Oy      1741 AOSGVPQFKKVVFOEFTDGSPTQPLXNGELNEHLGLCPYIRAEVEDNIMWTFRNOASR 1800
Db      1741 AOSGVPQFKKVVFOEFTDGSPTQPLXNGELNEHLGLCPYIRAEVEDNIMWTFRNOASR 1800
Oy      1801 PYSFSSLIISIEDDOGAEPKRNKVNKNEKTYFVKVQHNAAPTKDEFDCKAAVAFSDV 1860
Db      1801 PYSFSSLIISIEDDOGAEPKRNKVNKNEKTYFVKVQHNAAPTKDEFDCKAAVAFSDV 1860
Oy      1861 DLEKDVHSGILGPLYCHNTNLNPAHGOVYVGFALFTITDEKSMYFTENNERCA 1920
Db      1861 DLEKDVHSGILGPLYCHNTNLNPAHGOVYVGFALFTITDEKSMYFTENNERCA 1920
Oy      1921 PCNIOMEDEPTFEKENYRFAHNGYIMDTLPGLVMAQODRIRWYLLSMGSNENIHSIHSGH 1980
Db      1921 PCNIOMEDEPTFEKENYRFAHNGYIMDTLPGLVMAQODRIRWYLLSMGSNENIHSIHSGH 1980
Oy      1981 VETVAKKEEYKMAVLYMGVEYEVEMLPKAGIMRECELIQEHLHAQMYLPLVYSNKC 2040
Db      1981 VETVAKKEEYKMAVLYMGVEYEVEMLPKAGIMRECELIQEHLHAQMYLPLVYSNKC 2040
Oy      2041 QTPGLMASGHIRDFQITASGOYGAPKLABYSGSINAMSTKEPFSMIVDLAPMT 2100
Db      2041 QTPGLMASGHIRDFQITASGOYGAPKLABYSGSINAMSTKEPFSMIVDLAPMT 2100
Oy      2101 HGKTQGAROKFSSLYTISOPTIMYSLDCKKQTYRGNSGTGLMVFFGVNDSGKHNIFN 2160
Db      2101 HGKTQGAROKFSSLYTISOPTIMYSLDCKKQTYRGNSGTGLMVFFGVNDSGKHNIFN 2160
Oy      2161 PEIIRARYRLPHTYHSIRSTLMEELMGCDLNSCMLPGMESKAISDAOITASVYTMFA 2220
Db      2161 PEIIRARYRLPHTYHSIRSTLMEELMGCDLNSCMLPGMESKAISDAOITASVYTMFA 2220
Oy      2221 TWSPSKARHLQGRSNAMRPVNNKEMLOYDPKTKYTGVTGQVSKLTSMYKEFL 2280
Db      2221 TWSPSKARHLQGRSNAMRPVNNKEMLOYDPKTKYTGVTGQVSKLTSMYKEFL 2280
Oy      2281 ISSSDQGHQRTLPFGQKRYVQGSQDSFTYVNSLDPLLRIRYLRHPOSVQIALRM 2340
Db      2281 ISSSDQGHQRTLPFGQKRYVQGSQDSFTYVNSLDPLLRIRYLRHPOSVQIALRM 2340
Oy      2341 EYLGCEADQDLY 2351
Db      2341 EYLGCEADQDLY 2351

RESULT 19
ID AAM11427
XX AAM11427 standard; protein; 2351 AA.
AC AAM11427;
XX 20-NOV-1997 (first entry)
DE Active Factor VIII:C analogue, delta 1312, + Pro Insertion.
XX Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
XX fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
XX plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;
XX protocolytic cleavage.
OS Homo sapiens.
OS Synthetic.
XX Key
XX Peptide
XX Location/Qualifiers
FT 1..19
FT /note= "signal peptide"
FT 20..2351
FT /note= "mature Factor VIII:C"
FT Region
FT 20..1667
FT /note= "heavy chain fragment"
FT 1330..1331
FT Misc-difference
FT /note= "site of 1 residue deletion"

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FT	Modified-site	1331	/note= "inserted residue"
FT	Region	1668..2350	/note= "light chain fragment"
FT	Domain	760..1667	/note= "b domain"
FT			
PN	MO9703195-A1.		
XX			
PD	30-JAN-1997.		
XX			
PF	09-JUL-1996;	96MO-US11444.	
XX			
PR	11-JUL-1995;	95US-0001025.	
XX			
PA	(CHIR ) CHIRON CORP.		
XX			
PI	Cohen PE, Hung DT, Innis M;		
XX			
DR	WPI: 1997-119050/11.		
XX			
PT	Factor VIII:C analog modified adjacent to a non-activating Arg		
PT	residue - used in the treatment of haemophilias, by improvement of		
PT	haemostasis		
XX			
PS	Claim 29; Page -: 90pp; English.		
XX			
CC	AA011330-M1472 represent active Factor VIII:C analogues of the		
CC	invention. These sequences were created by mutating the wild type Factor		
CC	VIII:C coding sequence (see A451357) using mutagenic primers. The		
CC	analogues comprise a native Factor VIII:C polypeptide modified at a site		
CC	adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg		
CC	dipeptide is created. Factor VIII:C is a large glycoprotein that		
CC	participates in the blood coagulation cascade that ultimately converts		
CC	soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A		
CC	deficiency in Factor VIII:C is responsible for haemophilia A, which is an		
CC	X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is		
CC	activated by plasma proteases, such as thrombin. During activation the		
CC	mature polypeptide is cleaved to generate heavy and light chain fragments		
CC	that are further cleaved. Complexes of two or more of the analogues,		
CC	nucleic acids and vectors encoding them may be used alone or in		
CC	conjunction with each other, for the prevention or treatment of active		
CC	Factor VIII:C deficiency in a mammal. The analogues may be used as		
CC	immunogens to raise antibodies, and in the treatment of haemophilias, by		
CC	improvement of haemostasis. The analogues are resistant to proteolytic		
CC	cleavage and display increased plasma half-life. They may be administered		
CC	at lower dosages and by different modes of administration.		
CC			
SQ	Sequence	2351 AA:	
	Query Match	100.0%; Score 12412; DB 18; Length 2351;	
	Best local Similarity	100.0%; Pred. No. 0;	
	Matches 2350; Conservative	0; Mismatches	1; Indels
		0; Gaps	0;
Qy	1	MOELSTCFCLLRCSATRRYLGAVELSMDYMSDGLPEVDARPPRRVKSPPN	60
Db	1	MOELSTCFCLLRCSATRRYLGAVELSMDYMSDGLPEVDARPPRRVKSPPN	60
Qy	61	TSVYKKTLEFVETDHLFNIAKPRPMWGLGPTIOAEVYDVITLKNMASHVSLHAV	120
Db	61	TSVYKKTLEFVETDHLFNIAKPRPMWGLGPTIOAEVYDVITLKNMASHVSLHAV	120
Qy	121	GVSYWKASGEAEVDQTSOREKEDDKVPGGSHYVWQVLEKNGPMASDPLCTLYSLSH	180
Db	121	GVSYWKASGEAEVDQTSOREKEDDKVPGGSHYVWQVLEKNGPMASDPLCTLYSLSH	180
Qy	181	VDLYKDLNSGLIGALLVCRESGLAKETQTLHKTLFAVPDEGSKWSSEKNSLMDRD	240
Db	181	VDLYKDLNSGLIGALLVCRESGLAKETQTLHKTLFAVPDEGSKWSSEKNSLMDRD	240
Qy	241	AASARAPKMHYNGVYNSRLPGLIGCHRSKSVYWHVIGMOTTPVHSLTEGHTFLVRNH	300
Db	241	AASARAPKMHYNGVYNSRLPGLIGCHRSKSVYWHVIGMOTTPVHSLTEGHTFLVRNH	300

QY 1381 KGATQSPFSDCLTRSHSIPQANRSPDIAKVSSFPSIRPIYLRVLFQDNSSHLPAASY 1440  
DB 1381 KGATQSPFSDCLTRSHSIPQANRSPDIAKVSSFPSIRPIYLRVLFQDNSSHLPAASY 1440  
QY 1441 RKKGQVDESSHFLOGAKKNNLSLAITLLEMTGQQRVSGSLGTSATNSYTKKKEENTVLP 1500  
DB 1441 RKKGQVDESSHFLOGAKKNNLSLAITLLEMTGQQRVSGSLGTSATNSYTKKKEENTVLP 1500  
QY 1501 KPDLPTKSGKVELLPKVHIYQKDLPEPTETNSGPGHLDVDESLQGTGEGAIKKNEANRP 1560  
DB 1501 KPDLPTKSGKVELLPKVHIYQKDLPEPTETNSGPGHLDVDESLQGTGEGAIKKNEANRP 1560  
QY 1561 GVPPLRVATBSSAKTIPSKLLDPLAMDNHGTQIPKEEMKSOBKSPKTAFFKKDTLSL 1620  
DB 1561 GVPPLRVATBSSAKTIPSKLLDPLAMDNHGTQIPKEEMKSOBKSPKTAFFKKDTLSL 1620  
QY 1621 MACESNHAIAINEGONKPEIEVTWAKOGRTERLCSQNPVPLKRHOREITRTTQSDQEE 1680  
DB 1621 MACESNHAIAINEGONKPEIEVTWAKOGRTERLCSQNPVPLKRHOREITRTTQSDQEE 1680  
QY 1681 IDYDPTISEMKKEDPDVIDEDENOSPRSFOKTRHYFIAAVERLMDYGMSSSPHVLNR 1740  
DB 1681 IDYDPTISEMKKEDPDVIDEDENOSPRSFOKTRHYFIAAVERLMDYGMSSSPHVLNR 1740  
QY 1741 AOSGSVPQKVVYQETDQSTFOPLYRGELNEHLGLGPYIAEVEDINAVTRFNQASR 1800  
DB 1741 AOSGSVPQKVVYQETDQSTFOPLYRGELNEHLGLGPYIAEVEDINAVTRFNQASR 1800  
QY 1801 PYSFYSLSIYEEDOROGAERKNFVKNETKTYFMKVQHMAPTKDEFDCKANAYESDV 1860  
DB 1801 PYSFYSLSIYEEDOROGAERKNFVKNETKTYFMKVQHMAPTKDEFDCKANAYESDV 1860  
QY 1861 DLEKDVHSGLLGPLLVCHTNTLPAHGRQVYVQEFALFTIPETSKSWYFETENMERNCRA 1920  
DB 1861 DLEKDVHSGLLGPLLVCHTNTLPAHGRQVYVQEFALFTIPETSKSWYFETENMERNCRA 1920  
QY 1921 PCNIOMEDPTREKENTRRHAINGYINDTLRGLYAAQQRIRKTYLLSGSSENIHSHS9GH 1980  
DB 1921 PCNIOMEDPTREKENTRRHAINGYINDTLRGLYAAQQRIRKTYLLSGSSENIHSHS9GH 1980  
QY 1981 VFTVRRKKEEYKMALYNLYPGVFETVEMLPKAGIMRVDECLIGELHAGMSTLFLVYSNKC 2040  
DB 1981 VFTVRRKKEEYKMALYNLYPGVFETVEMLPKAGIMRVDECLIGELHAGMSTLFLVYSNKC 2040  
QY 2041 QPPLGASGHIRDFQITASGOYQOMAPKLARLHYSGSINAMSTKEPFSSIKVDLAPYII 2100  
DB 2041 QPPLGASGHIRDFQITASGOYQOMAPKLARLHYSGSINAMSTKEPFSSIKVDLAPYII 2100  
QY 2101 HGKTKOGAROKFSSLYISOFITMYSLDGKKQOTRGNSTGTLMVFFGNDSSGKIHNTFN 2160  
DB 2101 HGKTKOGAROKFSSLYISOFITMYSLDGKKQOTRGNSTGTLMVFFGNDSSGKIHNTFN 2160  
QY 2161 PPIIARIYRLPHPTYSIRSTLAMELMGCDLNSCSNPLGMSKASIDAOITASSYFTNFA 2220  
DB 2161 PPIIARIYRLPHPTYSIRSTLAMELMGCDLNSCSNPLGMSKASIDAOITASSYFTNFA 2220  
QY 2221 TWSPSKARLHJQGRSNMARPQVNNPKEMLOYDFOKTMYGVTTQGVKSLTSMVVKFEL 2280  
DB 2221 TWSPSKARLHJQGRSNMARPQVNNPKEMLOYDFOKTMYGVTTQGVKSLTSMVVKFEL 2280  
QY 2281 ISSSDQGHQWTLFPQNKVKVFEQGNDSFTPVNSLDPLLTLYRLHJQSWVHDIALRM 2340  
DB 2281 ISSSDQGHQWTLFPQNKVKVFEQGNDSFTPVNSLDPLLTLYRLHJQSWVHDIALRM 2340  
QY 2341 EYLGECAQDLY 2351  
DB 2341 EYLGECAQDLY 2351

RESULT 20  
AAW11408  
ID AAW11408 standard; Protein: 2351 AA.  
XX

AC AAW11408:  
XX 20-NOV-1997 (first entry)  
XX Active Factor VIII:C analogue, delta 777, + residue 777 insertion.  
DE Factor VIII:C: analogue; glycoprotein; blood coagulation cascade;  
XX fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KW plasma protease; thrombin; immunogen; antibody; haemophilias; therapy;  
XX proteolytic cleavage.  
OS Homo sapiens.  
OS Synthetic.  
XX  
XX Key location/Qualifiers  
FH 1..19  
FH Peptide /note= "signal peptide"  
FT 20..2351  
FT Protein /note= "mature Factor VIII:C"  
FT 20..1667  
FT Region /note= "heavy chain fragment"  
FT Misc-difference /note= "site of 1 residue deletion"  
FT 795..796  
FT Modified-site /note= "inserted residue, optionally deleted"  
FT Region /note= "2350  
FT 1668..2350  
FT 760..1667  
FT Domain /note= "B domain"  
XX W09703195-A1.  
XX 30-JAN-1997.  
XX 09-JUL-1996; 96WO-US11444.  
XX 11-JUL-1995; 95US-0001025.  
XX (CHIR ) CHIRON CORP.  
XX Cohen FE, Hung DT, Innis M;  
XX WPI; 1997-119050/11.  
XX Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophilias, by improvement of  
PT haemostasis  
XX  
XX Claim 25; Page -: 90pp; English.  
XX AAW11330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAW15157) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophilias, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX Sequence 2351 AA:

Query Match	100.0%	Score 12412	DB 18	Length 2351
Best Local Similarity	100.0%	Pred. No. 0		
Matches 2350	Conservative 0	Mismatches 1	Indels 0	Gaps 0
Qy	1	MOIELSTCFPLCLLRFCFSATRRYLGAVELSMYQMSDGLPDAFPPRRVKSPPFN 60		
Db	1	MOIELSTCFPLCLLRFCFSATRRYLGAVELSMYQMSDGLPDAFPPRRVKSPPFN 60		
Qy	61	TSVYKKTLEFERTDLFNIAKPRPMGGLPTIOAEYDVTVTLKMSASHVSLAHN 120		
Db	61	TSVYKKTLEFERTDLFNIAKPRPMGGLPTIOAEYDVTVTLKMSASHVSLAHN 120		
Qy	121	GVSYWKASGAEXDDOTSQREKEDDKYPPGGSHYVQVYLKENGPMASDPLCLTYSLAH 180		
Db	121	GVSYWKASGAEXDDOTSQREKEDDKYPPGGSHYVQVYLKENGPMASDPLCLTYSLAH 180		
Qy	181	VDLYKDLNSGLIGALLVCREGSLAKEKOTLHKFILLFVFDGKSWHSETKNSLMQDRD 240		
Db	181	VDLYKDLNSGLIGALLVCREGSLAKEKOTLHKFILLFVFDGKSWHSETKNSLMQDRD 240		
Qy	241	AASARAMPKHTVNGVYVNSLPGLIGHKRSVYWHYVIGMGTPEVHSLFLEGHTFLVRNH 300		
Db	241	AASARAMPKHTVNGVYVNSLPGLIGHKRSVYWHYVIGMGTPEVHSLFLEGHTFLVRNH 300		
Qy	301	ROASLEISPTFLTAOTLLMDLGOFLRCHTSSHODHGMBAVYKYVDSCEPEERPOLRMKNNE 360		
Db	301	ROASLEISPTFLTAOTLLMDLGOFLRCHTSSHODHGMBAVYKYVDSCEPEERPOLRMKNNE 360		
Qy	361	EAEDYDDDLTDSMDVYRFDDDNPSFTQIRSVYKAKKPKTWYHIAAEEDMDVAPLYLA 420		
Db	361	EAEDYDDDLTDSMDVYRFDDDNPSFTQIRSVYKAKKPKTWYHIAAEEDMDVAPLYLA 420		
Qy	421	PDDRSYKSOYLNNGPORIGRKKYKREMAVDEPFKREAIQHEGSLIGLLYEVDLT 480		
Db	421	PDDRSYKSOYLNNGPORIGRKKYKREMAVDEPFKREAIQHEGSLIGLLYEVDLT 480		
Qy	481	LIIERKNOASRPYNIYPHGITDVPRLYSRRLPKGVKHLKDPILLPGIRFKYKWTYVEDG 540		
Db	481	LIIERKNOASRPYNIYPHGITDVPRLYSRRLPKGVKHLKDPILLPGIRFKYKWTYVEDG 540		
Qy	541	TKSDPRCLTRYSSFFNMNERDLASGLIPLLICIKESVDORGNOIJSKRVNLIJFSVDE 600		
Db	541	TKSDPRCLTRYSSFFNMNERDLASGLIPLLICIKESVDORGNOIJSKRVNLIJFSVDE 600		
Qy	601	NRSWYFENTIORELPAPAGVQLEDPERQASNMHSTNGVYFDSLOSLQCLHEVAHWILS 660		
Db	601	NRSWYFENTIORELPAPAGVQLEDPERQASNMHSTNGVYFDSLOSLQCLHEVAHWILS 660		
Qy	661	IGAQTDFLSVFFSGYTFKHKWYEDTLTLFPFSGEIVFMSMENPGIWLGC HNSDFNRNG 720		
Db	661	IGAQTDFLSVFFSGYTFKHKWYEDTLTLFPFSGEIVFMSMENPGIWLGC HNSDFNRNG 720		
Qy	721	MTALTKVSSCDKNTGVOYEDSYEDISAYLLSKNNAIEPRFSQNSHSPSTQOKOFNATTI 780		
Db	721	MTALTKVSSCDKNTGVOYEDSYEDISAYLLSKNNAIEPRFSQNSHSPSTQOKOFNATTI 780		
Qy	781	PENDIEKTDMPFAHRPMPKRIQNVSSDMLMLKQSPTPRGJLSLDQAEKTEFPDDPS 840		
Db	781	PENDIEKTDMPFAHRPMPKRIQNVSSDMLMLKQSPTPRGJLSLDQAEKTEFPDDPS 840		
Qy	841	PGALDSNNSLSEMHFRPOLHHSGLDMVTPESGLQRLNLEKLGTTAATELKLDFKVSST 900		
Db	841	PGALDSNNSLSEMHFRPOLHHSGLDMVTPESGLQRLNLEKLGTTAATELKLDFKVSST 900		
Qy	901	SNNLSTIPSDNLAAGDNTSSLGPPSMRVHYDOLDLTLTFGKKSPLTESGGPLSTSEE 960		
Db	901	SNNLSTIPSDNLAAGDNTSSLGPPSMRVHYDOLDLTLTFGKKSPLTESGGPLSTSEE 960		
Qy	961	NNDSKLIESGLMNSQSSGKAVSSTESGRLFKCKRAHGALLTKDNALFYVSIJLKTN 1020		
Db	961	NNDSKLIESGLMNSQSSGKAVSSTESGRLFKCKRAHGALLTKDNALFYVSIJLKTN 1020		
Qy	1021	KTSNNSATNRKTHIDPSSLIENSPOVQNIJESDTEFKKVTPLIHDMRLMDKNAATLRL 1080		

Db	1021	KTSNNSATNRKTHIDPSSLIENSPOVQNIJESDTEFKKVTPLIHDMRLMDKNAATLRL 1080		
Qy	1081	NHMSNKTSSKNMENVQOKKEGPJPPDAQNPDMSPFKMLFLPESARWIOPTHGKNSLNSG 1140		
Db	1081	NHMSNKTSSKNMENVQOKKEGPJPPDAQNPDMSPFKMLFLPESARWIOPTHGKNSLNSG 1140		
Qy	1141	QGPSKOLVSLGPEKVEBQONFLSEKKKVVYVGGEPFTKVGLKEVFPSSNLFJNLND 1200		
Db	1141	QGPSKOLVSLGPEKVEBQONFLSEKKKVVYVGGEPFTKVGLKEVFPSSNLFJNLND 1200		
Qy	1201	LHENNTNDEKTOIEIEKEKTELIOENVVLPOIHTYTGKTNKMLFLSTROVGESTD 1260		
Db	1201	LHENNTNDEKTOIEIEKEKTELIOENVVLPOIHTYTGKTNKMLFLSTROVGESTD 1260		
Qy	1261	GAYAPVLQDFRSLNDSTNRKTHAHFSKGEEDNEGLGNQTKOYEVKACTRISPTN 1320		
Db	1261	GAYAPVLQDFRSLNDSTNRKTHAHFSKGEEDNEGLGNQTKOYEVKACTRISPTN 1320		
Qy	1321	SOQNFVTOBKRALKQFLPEETELKRTIYDSTQSKMKHLPPSTLTQIDYNEKE 1380		
Db	1321	SOQNFVTOBKRALKQFLPEETELKRTIYDSTQSKMKHLPPSTLTQIDYNEKE 1380		
Qy	1381	KGATQSPISDCLTRSHSIPQANRSPLEIAKVSFSPSIRPYLTVFVLEFQDNSSHLPAAS 1440		
Db	1381	KGATQSPISDCLTRSHSIPQANRSPLEIAKVSFSPSIRPYLTVFVLEFQDNSSHLPAAS 1440		
Qy	1441	RKKGVSQVESHPLOQAKKNLISALITLLEMTGDOREVSGLQTSATNSVTYKKEVNTVLP 1500		
Db	1441	RKKGVSQVESHPLOQAKKNLISALITLLEMTGDOREVSGLQTSATNSVTYKKEVNTVLP 1500		
Qy	1501	KPDLPKTSGVELLPVHTYOKDLPEFTSNGSGHLDLYEGLLOGTGEGAKKNEANRP 1560		
Db	1501	KPDLPKTSGVELLPVHTYOKDLPEFTSNGSGHLDLYEGLLOGTGEGAKKNEANRP 1560		
Qy	1561	GKVPPLVYATESSAKTPSKLLDPLANDNHGTOIPKEBKESQEKSPBETAKKODTILS 1620		
Db	1561	GKVPPLVYATESSAKTPSKLLDPLANDNHGTOIPKEBKESQEKSPBETAKKODTILS 1620		
Qy	1621	NACESHNAIAINEGONKPEIEVYAKQRTERLCSQNPVYLKRHQREITRTTLOSDOE 1680		
Db	1621	NACESHNAIAINEGONKPEIEVYAKQRTERLCSQNPVYLKRHQREITRTTLOSDOE 1680		
Qy	1681	IDYDDTISVEMKKEDDIYDEBENSPPSPQKTRHYFLAAVERLMDYGMSSPHVLRNR 1740		
Db	1681	IDYDDTISVEMKKEDDIYDEBENSPPSPQKTRHYFLAAVERLMDYGMSSPHVLRNR 1740		
Qy	1741	AQSGSVPOFKKVVYPOEFTDGSFTQPLYRGEJLNEHLGLGPTYRAEVEDNIMVTRNOASH 1800		
Db	1741	AQSGSVPOFKKVVYPOEFTDGSFTQPLYRGEJLNEHLGLGPTYRAEVEDNIMVTRNOASH 1800		
Qy	1801	PYSFVSSLIISYEDQOGAEPKRNKVPKNETKTYFKWVOHNAPTKDEDFDCAKAAVPSDV 1860		
Db	1801	PYSFVSSLIISYEDQOGAEPKRNKVPKNETKTYFKWVOHNAPTKDEDFDCAKAAVPSDV 1860		
Qy	1861	DLEKDVHSGILGFLVCHNTNLNPAHGOVYVOEFLPFIIDETKSYVFPENNERCRA 1920		
Db	1861	DLEKDVHSGILGFLVCHNTNLNPAHGOVYVOEFLPFIIDETKSYVFPENNERCRA 1920		
Qy	1921	PCNIQMEDPTFKENYFRAINCYIMDTLPGJLWMAODRIRMTWLSMGSNENIHSIFSGH 1980		
Db	1921	PCNIQMEDPTFKENYFRAINCYIMDTLPGJLWMAODRIRMTWLSMGSNENIHSIFSGH 1980		
Qy	1981	VFTYRKKEEYKMAIYLVGVEFTEYEMLPKSAKGIWRECLIGEBLHAQMSLFLVYSNKC 2040		
Db	1981	VFTYRKKEEYKMAIYLVGVEFTEYEMLPKSAKGIWRECLIGEBLHAQMSLFLVYSNKC 2040		
Qy	2041	QTPJGMAASHIHDPOTTASGQGOAARLARIYSSISINAASTKEPESWITKYDILAPMIT 2100		
Db	2041	QTPJGMAASHIHDPOTTASGQGOAARLARIYSSISINAASTKEPESWITKYDILAPMIT 2100		
Qy	2101	HGKTGQARQFSSSLYISOFIIMYSLDGKKQWYRGNSGTGLMVEFGVNDSSGIKHNIFN 2160		
Db	2101	HGKTGQARQFSSSLYISOFIIMYSLDGKKQWYRGNSGTGLMVEFGVNDSSGIKHNIFN 2160		

Db	2101	HGICVQARQKFSLSYISQFIIMVSLDGKWKQYRENSIGTLMPFQGNVDSGSIKKNIN	2160
Qy	2161	PTIARIRLRHPHNSIRSTLRMLMGCDLNSGSMPLGMSKATSDAOIRASSYFTNMA	2220
Db	2161	PTIARIIRLRHPHNSIRSTLRMLMGCDLNSGSMPLGMSKATSDOIRASSYFTNMA	2220
Qy	2221	TWSPSKARLHLQGRSNAMRPVNNPKEMLOVDFOKTMKVTGVITQGVKSLTSMYKEFL	2280
Db	2221	TWSPSKARLHLQGRSNAMRPVNNPKEMLOVDFOKTMKVTGVITQGVKSLTSMYKEFL	2280
Qy	2281	ISSSQDQHQTTLFFQNGKVKYFQGNODSPFPVNSLDPPLRLIRLHPQSWHQAIALRM	2340
Db	2281	ISSSQDQHQTTLFFQNGKVKYFQGNODSPFPVNSLDPPLRLIRLHPQSWHQAIALRM	2340
Qy	2341	EVLCGEADQLY 2351	
Db	2341	EVLCGEADQLY 2351	
RESULT 21			
AAW11347			
ID	AAW11347	standard; Protein; 2351 AA.	
AC	AAW11347;		
DT	17-NOV-1997	(first entry)	
DE	Active Factor VIII:C analogue K251P.		
KM	Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;		
KW	fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;		
KM	plasma protease; thrombin; immunogen; antibody; haemophilia; therapy;		
KW	proteolytic cleavage.		
OS	Homo sapiens.		
OS	Synthetic.		
XX	Key	Location/Qualifiers	
XX	Peptide	1..19	
XX	Protein	/note="signal peptide"	
XX	Region	20..2351	
XX	Modified-site	/note="mature Factor VIII:C"	
XX	Region	20..1667	
XX	Region	/note="heavy chain fragment"	
XX	Domain	/label="K251P"	
XX	Domain	1668..2350	
XX	Domain	/note="light chain fragment"	
XX	Domain	760..1667	
XX	Domain	/note="B domain"	
XX	NO9703195-RL.		
XX	30-JAN-1997.		
XX	09-JUL-1996;	96WO-US11444.	
XX	11-JUL-1995;	95US-0001025.	
XX	(CHIR ) CHIRON CORP.		
XX	Cohen FE, Hung DT, Innis M;		
XX	WPI; 1997-119050/11.		
XX	Factor VIII:C analog modified adjacent to a non-activating Arg		
XX	residue - used in the treatment of haemophiliacs, by improvement of		
XX	hemostasis		
XX	Claim 11: Page -; 90pp; English.		
XX	AAW11330-W11472	represent active Factor VIII:C analogues of the	
XX	invention. These sequences were created by mutating the wild type Factor		

CC	VIII:C binding sequence (see A6U5157) using mitogenic primers. The
CC	analogues comprise a native factor VIII:C polypeptide modified at a site
CC	adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC	dipeptide is created. Factor VIII:C is a large glycoprotein that
CC	participates in the blood coagulation cascade that ultimately converts
CC	soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC	deficiency in Factor VIII:C is responsible for hemophilia A, which is an
CC	X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC	activated by plasma proteases, such as thrombin. During activation the
CC	mature polypeptide is cleaved to generate heavy and light chain fragments
CC	that are further cleaved. Complexes of two or more of the analogues,
CC	nucleic acids and vectors encoding them may be used alone or in
CC	conjunction with each other, for the prevention or treatment of active
CC	Factor VIII:C deficiency in a mammal. The analogues may be used as
CC	immunogens to raise antibodies, and in the treatment of haemophilias, by
CC	improvement of haemostasis. The analogues are resistant to proteolytic
CC	cleavage and display increased plasmas half-life. They may be administered
CC	at lower dosages and by different modes of administration.
XX	
SQ	Sequence 2351 AA:
	Query Match 100.0%; Score 12412; DB 18; Length 2351;
	Best Local Similarity 100.0%; Pred. No. 0;
	Matches 2350; Conservative 0; Mismatches 1; Indels 0; Gaps 0
OY	1 MOELSTFFCLTRFCFSATRRYYLGAVELSMVDSMDGELPVDARPPRPVKSPFN 60
DB	1 MOELSTCFCLLRFCSFATRRYYLGAVELSMVDSMDGELPVDARPPRPVKSPFN 60
OY	TSVYVKTLPEFPDHLFNAIKRPRPMGLGPITDAEYDVTVTLKNMASHVSJAHV 120
DB	TSVYVKTLPEFPDHLFNAIKRPRPMGLGPITDAEYDVTVTLKNMASHVSJAHV 120
OY	GVSYKASGEAEYDDQSOREKEEDKVPGSSHYVMQLAKNGPSADPLCTLYSLH 180
DB	GVSYKASGEAEYDDQSOREKEEDKVPGSSHYVMQLAKNGPSAPCLCTLYSLH 180
OY	VDLVNDLSGLIGALLVCREGSLAKEKTQTLLKFIILFAVFDEGSKSWHSETKNSLMODRD 240
DB	VDLVNDLSGLIGALLVCREGSLAKEKTQTLLKFIILFAVFDEGSKSWHSETKNSLMODRD 240
OY	AASARAMPKMTGVGYNRSRLPCGLICGRKASYVMNVIGMOTTPREHNSIFLGHPFLVRNH 300
DB	AASARAMPKMTGVGYNRSRLPCGLICHRPSVMNVIGMOTTPREVSIETLGHPFLVRNH 300
OY	ROASEIPIPTFFLAQRLLMLDGOFLELCCHISSHQHGMGAAYKVDCSCEEPOLRMKNE 360
DB	RQASEIPIPTFFLAQRLLMLDGOFLELCCHISSHQHGMGAAYKVDCSCPEEPOLRMKNE 360
OY	EAEVDYDDLTSBMDVVRPDONSSEFTIOISVAKHKPKMKMYIAAEEEDMVADAPLYLA 420
DB	EAEVDYDDLTSBMDVVRFDONSSSFIOISVAKHKPKMYIAAEBEDMVADAPLYLA 420
OY	PDDRSTKSQVLYNNPDRIGRKRYKKAFMAAYIDDEFKTRERLOHESLSIGLPPLYEGVEDTL 480
DB	PDDRSTKSQVLYNNPDRIGRKRYKKAFMAAYIDDEFKTRERLOHESLSIGLPPLYEGVEDTL 480
OY	LILFRNQMSRENYIPGIGINDVAPLYSRRLRGVYKLKADPLLPGEIFEKWTVYEDGP 540
DB	LILFRNQMSRENYIPGIGINDVAPLYSRRLRGVYKLKADPLLPGEIFEKWTVYEDGP 540
OY	TKSDPCLSTRYSFYMNERDLASGLIGLLCYCKESVDNRGNQIMSDRVNLIFYSVDE 6000
DB	TKSDPCLSTRYSFYMNERDLASGLIGLLCYCKESVDNRGNQIMSDRVNLIFYSVDE 6000
OY	NBSXYLTENIORPLPNAGVOLDEDPFOASNTHMSGVGFDSLQSYCNLEHVAYWTLS 660
DB	NBSXYLTENIORPLPNAGVOLDEPFQASNTHMSGVGFDSLQSYCNLEHVAYWTLS 660
OY	IGAQTDLSVFESSGYTFRKMAYEDTLTLPFPSCSEIVKSNENPGILMGCHNSDFNRKG 720
DB	IGAQTDLSVFESSGYTFRKMAYEDTLTLPFPSCSEIVKSNENPGILMGCHNSDFNRKG 720



QY 721 MTALLKVSCKNKTG DYEDSYEDISAYLLSKNNAIEPRSFQNSRHRPSTRKOKFNATTI 780  
DB 721 MTALLKVSCKNKTG DYEDSYEDISAYLLSKNNAIEPRSFQNSRHRPSTRKOKFNATTI 780  
QY 761 PENDIEKTPWFARHPMPKIQIONVSSDDLMLRQSPPHGISLSLDIOEAKYEFESDDPS 840  
DB 761 PENDIEKTPWFARHPMPKIQIONVSSDDLMLRQSPPHGISLSLDIOEAKYEFESDDPS 840  
QY 841 PGALDSNNLSSEMTFRQLHHSQDMVFTPESQLRLNEKIGTTAATLKKLDPKVYSST 900  
DB 841 PGALDSNNLSSEMTFRQLHHSQDMVFTPESQLRLNEKIGTTAATLKKLDPKVYSST 900  
QY 901 SNNLSTIPSDNLAACTDNTSSLGPPSMVHYDSQDLDTTLFGKSSPLTESGGPLSIEE 960  
DB 901 SNNLSTIPSDNLAACTDNTSSLGPPSMVHYDSQDLDTTLFGKSSPLTESGGPLSIEE 960  
QY 961 NNDSKLLESGLMSQESSMGNVSTESGRLFGKRAHGPALLTKDNALFKVSTSLKTN 1020  
DB 961 NNDSKLLESGLMSQESSMGNVSTESGRLFGKRAHGPALLTKDNALFKVSTSLKTN 1020  
QY 1021 KTSNNSATNRKTHIDQPSLLIENSPVWONTLESOTFEKKVTPLIHDMMLDKNATRL 1080  
DB 1021 KTSNNSATNRKTHIDQPSLLIENSPVWONTLESOTFEKKVTPLIHDMMLDKNATRL 1080  
QY 1081 NMSNKTTSKKNMEMVQOKKEGPJPPDAONPDMSFFKMLFLESARWIOPTHGKNSLNSG 1140  
DB 1081 NMSNKTTSKKNMEMVQOKKEGPJPPDAONPDMSFFKMLFLESARWIOPTHGKNSLNSG 1140  
QY 1141 QGSPKOLVSLGPEKEVEGONFLSEKKNVYVGGEFTKDVGLKEMVPPSSNNLFLTNLD 1200  
DB 1141 QGSPKOLVSLGPEKEVEGONFLSEKKNVYVGGEFTKDVGLKEMVPPSSNNLFLTNLD 1200  
QY 1201 LHENNTNOKKIQOEIEIEKKEFTLQENNVYLPQIHVYTGKNMKMLFLLSTRQVBSVD 1260  
DB 1201 LHENNTNOKKIQOEIEIEKKEFTLQENNVYLPQIHVYTGKNMKMLFLLSTRQVBSVD 1260  
QY 1261 GAYAPVLQDFRSLNDSTNRTKHTAHFSKKEEENLEGLNQTOKIWEKVACTTRISPN 1320  
DB 1261 GAYAPVLQDFRSLNDSTNRTKHTAHFSKKEEENLEGLNQTOKIWEKVACTTRISPN 1320  
QY 1321 SOONPVTORSKRALKOFRLPLEETLEKRIIYVDTSTQMSKMKHLPPSTLTQIDYNEKE 1380  
DB 1321 SOONPVTORSKRALKOFRLPLEETLEKRIIYVDTSTQMSKMKHLPPSTLTQIDYNEKE 1380  
QY 1381 KGAITQSPSLDCLTRSHSTIPQANRSPLEIAKVSSFPISIRIYLTLYVLQODNSHLPAASY 1440  
DB 1381 KGAITQSPSLDCLTRSHSTIPQANRSPLEIAKVSSFPISIRIYLTLYVLQODNSHLPAASY 1440  
QY 1441 RKKDSGOESSHFLQGAKKNNLSLAILLEMTGDQREVSGLSGTSATNSVTYKKEENTVLP 1500  
DB 1441 RKKDSGOESSHFLQGAKKNNLSLAILLEMTGDQREVSGLSGTSATNSVTYKKEENTVLP 1500  
QY 1501 KPDLKTSKGVVLLPVRHYHOKDLPPTSGSGHLDVESSLQGEKIKKNEANRP 1560  
DB 1501 KPDLKTSKGVVLLPVRHYHOKDLPPTSGSGHLDVESSLQGEKIKKNEANRP 1560  
QY 1561 GKVPFLVATRESSAKTPSKLIDPLAMDNHYGTQIPKEKMSQEKSPERTAKKKDTLLST 1620  
DB 1561 GKVPFLVATRESSAKTPSKLIDPLAMDNHYGTQIPKEKMSQEKSPERTAKKKDTLLST 1620  
QY 1621 NACESNHAIAINEGONKPEIEVTAQKQFERKCSQNPVLKRQORETTRTQSOOE 1680  
DB 1621 NACESNHAIAINEGONKPEIEVTAQKQFERKCSQNPVLKRQORETTRTQSOOE 1680  
QY 1681 IDYDDTISVEMKKEEDPDIYDEENQSPRSFQKTRHAFIAAVERLMDGMSSSHVILNR 1740  
DB 1681 IDYDDTISVEMKKEEDPDIYDEENQSPRSFQKTRHAFIAAVERLMDGMSSSHVILNR 1740  
QY 1741 AQSQSVPOFKKVVFOEFTDGSFTQPLRGELNEHLGLGPIYRAVEDNINWVTRNOASR 1800  
DB 1741 AQSQSVPOFKKVVFOEFTDGSFTQPLRGELNEHLGLGPIYRAVEDNINWVTRNOASR 1800  
QY 1801 PYSFVSSLSIEEDQOGAEPKRNKVRKNEKITYFMKVQHHAHPKDFEODCKAAYFSDV 1860

DB 1801 PYSFVSSLSIEEDQOGAEPKRNKVRKNEKITYFMKVQHHAHPKDFEODCKAAYFSDV 1860  
QY 1861 DLEKDVHSGILGPLVCHTNTLNPABHROVYVOERAPLFTTJEDFKSMYETEMNERNCA 1920  
DB 1861 DLEKDVHSGILGPLVCHTNTLNPABHROVYVOERAPLFTTJEDFKSMYETEMNERNCA 1920  
QY 1921 PCNTOMEDPFEKENTRFAHNGYIMDFLPELVAAQORIRMYLLSMGSNNHISHFSGH 1980  
DB 1921 PCNTOMEDPFEKENTRFAHNGYIMDFLPELVAAQORIRMYLLSMGSNNHISHFSGH 1980  
QY 1981 VFVYRKKEEYKALNLYPYFEFVENLPSKAGIYRVECLIGELHAGMSTLFLVYSNKC 2040  
DB 1981 VFVYRKKEEYKALNLYPYFEFVENLPSKAGIYRVECLIGELHAGMSTLFLVYSNKC 2040  
QY 2041 QTPLGMASSHIRDFQITRASGOYQOMAKRLARLHYSGSJINAMSTKEPESWIRVDLAPMII 2100  
DB 2041 QTPLGMASSHIRDFQITRASGOYQOMAKRLARLHYSGSJINAMSTKEPESWIRVDLAPMII 2100  
QY 2101 HGITQGARQKFSLSYISQFTIMYSLDGKKWQYRGNSTGTLMVFPGVNDSGIRKINIFN 2160  
DB 2101 HGITQGARQKFSLSYISQFTIMYSLDGKKWQYRGNSTGTLMVFPGVNDSGIRKINIFN 2160  
QY 2161 PPIIARIIRLPHTHSINSTLRMELACDINSGSMPLGHEKSAISDAQITRASSYFTNMA 2220  
DB 2161 PPIIARIIRLPHTHSINSTLRMELACDINSGSMPLGHEKSAISDAQITRASSYFTNMA 2220  
QY 2221 TWSPSKARLHLQGRSNAMRPQNNPKEMLOVDFOKTMKVYGTQGVKSLTSMYKEFL 2280  
DB 2221 TWSPSKARLHLQGRSNAMRPQNNPKEMLOVDFOKTMKVYGTQGVKSLTSMYKEFL 2280  
QY 2281 ISSQDGHQWTLFFQNGYKVFQGNQSFPPVNSLDPPLRLRYRRIHPOSVYHOTALM 2340  
DB 2281 ISSQDGHQWTLFFQNGYKVFQGNQSFPPVNSLDPPLRLRYRRIHPOSVYHOTALM 2340  
QY 2341 EYLCEAODLY 2351  
DB 2341 EYLCEAODLY 2351  
RESULT 22  
ID AAM11332 standard; protein; 2351 AA.  
XX AAM11332;  
AC 17-NOV-1997 (first entry)  
DT XX  
DE Active Factor VIII:C analogue Q218X.  
KW Factor VIII:C; analogue; glycoprotein; blood coagulation cascade; fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis; plasma protease; thrombin; immunogen; antibody; haemophilic; therapy; proteolytic cleavage.  
OS Homo sapiens.  
XX Synthetic.  
XX  
FH Key 1..19 Location/Qualifiers  
FT Peptide /note= "signal peptide"  
FT Protein 20..2351  
FT /note= "mature Factor VIII:C"  
FT Region 20..1667  
FT /note= "heavy chain fragment"  
FT Modified-site 237  
FT /label= Phe, Glu, Pro  
FT Region 1668..2350  
FT /note= "light chain fragment"  
FT 760..1667  
FT /note= "b domain"  
XX  
PN MO9703195-A1.



[illegible]

Oy	421	PDDBSKYSQJLNNNGPORIORIKKAKKRYPMATYDDEFTFTRALIOHESGILGJLGLYGEVOTL	480
Oy	422	PDDBSKYSQJLNNNGPORIORIKKAKKRYPMATYDDEFTFTRALIOHESGILGJLGLYGEVOTL	480
Db	421	PDDBSKYSQJLNNNGPORIORIKKAKKRYPMATYDDEFTFTRALIOHESGILGJLGLYGEVOTL	480
Oy	481	LIIFFKNOASRPNIYPHGJITDVRPLYSRRLPKGVKHLKDPILDEGEIFKKYKMTVYEDGP	540
Db	481	LIIFFKNOASRPNIYPHGJITDVRPLYSRRLPKGVKHLKDPILDEGEIFKKYKMTVYEDGP	540
Oy	541	TKSDPRLCTRYYSAPFNMERDLASGLGJLPLICYKESYQORONQJMSDKRNVLFSVEDE	600
Db	541	TKSDPRLCTRYYSAPFNMERDLASGLGJLPLICYKESYQORONQJMSDKRNVLFSVEDE	600
Oy	601	NKSWYLTENTIOREFLPPMAPVOLEDEPEQASIMHSJNGVFPISJOLSYCICHEVAYUYJLS	660
Db	601	NKSWYLTENTIOREFLPPMAPVOLEDEPEQASIMHSJNGVFPISJOLSYCICHEVAYUYJLS	660
Oy	661	ICAOQDFLSVFPSCGYTFKKHKMYEDOTLTLPPSGEYVPMSENBOLMILGCHMSDRNNG	720
Db	661	ICAOQDFLSVFPSCGYTFKKHKMYEDOTLTLPPSGEYVPMSENBOLMILGCHMSDRNNG	720
Oy	721	MTALLKVVSCDKNTGYEDYSYEDISAYLLSKNNAIEPPRSFSONRHPSTROKOFNATTI	780
Db	721	MTALLKVVSCDKNTGYEDYSYEDISAYLLSKNNAIEPPRSFSONRHPSTROKOFNATTI	780
Oy	781	PENDIEKTDPEFAHRIPMKRIOWNSSJOLMLJROSPFPHGJLSJDLQEAKEYTEFDDBS	840
Db	781	PENDIEKTDPEFAHRIPMKRIOWNSSJOLMLJROSPFPHGJLSJDLQEAKEYTEFDDBS	840
Oy	841	PAIDSNNSJSEMHTRPRLHSHGGMVTPESGJOLRLMKJIGTAAATELKIIDLFPVST	900
Db	841	PAIDSNNSJSEMHTRPRLHSHGGMVTPESGJOLRLMKJIGTAAATELKIIDLFPVST	900
Oy	901	SNMLISTIPSDNLAAGTDWSSLGPPSPHAYHYSQJDLTLTFGKSSPLTESGGLSLSSE	960
Db	901	SNMLISTIPSDNLAAGTDWSSLGPPSPHAYHYSQJDLTLTFGKSSPLTESGGLSLSSE	960
Oy	961	NNDKSLTESGJLMSQESSSGKNVSSSTESGRLFGKRAHAPALLTRKDNALFKVYSISLKTN	1020
Db	961	NNDKSLTESGJLMSQESSSGKNVSSSTESGRLFGKRAHAPALLTRKDNALFKVYSISLKTN	1020
Oy	1021	KTSNNSAINRRTXTHIDSPSLJINENSVMQNTLESJDEFEKKVPLPLIHBYMLMDXNNATALRL	1080
Db	1021	KTSNNSAINRRTXTHIDSPSLJINENSVMQNTLESJDEFEKKVPLPLIHBYMLMDXNNATALRL	1080
Oy	1081	NHMSKNTTSSKNMBMYOQKKEGRTPPDQONDMSFFKMLFIPESARWJORTHKNLSLNSG	1140
Db	1081	NHMSKNTTSSKNMBMYOQKKEGRTPPDQONDMSFFKMLFIPESARWJORTHKNLSLNSG	1140
Oy	1141	OQSPKOLYSLGPEKSYEQONFLSKKNVYVGGEETKRYGLAKEMVFPSSKNLFTJNLN	1200
Db	1141	OQSPKOLYSLGPEKSYEQONFLSKKNVYVGGEETKRYGLAKEMVFPSSKNLFTJNLN	1200
Oy	1201	LHEHNTNHOEKKIOEBELKEKTLIOENVNLPOJHJYVGTKNFMKNLFLJLSTRONVEGSYD	1260
Db	1201	LHEHNTNHOEKKIOEBELKEKTLIOENVNLPOJHJYVGTKNFMKNLFLJLSTRONVEGSYD	1260
Oy	1261	GAYAVYLDQFSLSDSYNTRKKHTAHFSKKEEBENLEGJNTRQIYEKYACTTRISPT	1320
Db	1261	GAYAVYLDQFSLSDSYNTRKKHTAHFSKKEEBENLEGJNTRQIYEKYACTTRISPT	1320
Oy	1321	SOONVYORSKRALKORPLRETELEKRIIVYDTSPQSKMMKMLPSTLTIOIDYNEKE	1380
Db	1321	SOONVYORSKRALKORPLRETELEKRIIVYDTSPQSKMMKMLPSTLTIOIDYNEKE	1380
Oy	1381	KGAITOSPJLSDCLTRSHSTIPQANRSPRLIAKVSSPSPIRYLTUVRLEPQDNSSHLPAASY	1440
Db	1381	KGAITOSPJLSDCLTRSHSTIPQANRSPRLIAKVSSPSPIRYLTUVRLEPQDNSSHLPAASY	1440
Oy	1441	RKDDSGVOESSHFJOGAKKNNLSJLILILEMTGQDORVSGJLQTSATNVSYTKRYENTVPL	1500
Db	1441	RKDDSGVOESSHFJOGAKKNNLSJLILILEMTGQDORVSGJLQTSATNVSYTKRYENTVPL	1500

Thu Jul 3 11:46:09 2003

np-000123.rag

immunogen: antibody: haemophilic: therapy:

[illegible][illegible]

Db	61	TSVYKKTLEFVEETHLFINIAKRPPEMGLIGPTIOAEVYDTVYITLKNASHPVLSHA	120
Qy	121	GVSYWKASGEAYDQTSQREKEDDKVPGGSHYVWQVLKENGPAADPLCLTYSYLSH	180
Db	121	GVSYWKASGEAYDQTSQREKEDDKVPGGSHYVWQVLKENGPAADPLCLTYSYLSH	180
Qy	181	VDLYKDLNSGLIGALLVCREGSLAKEKQTLAKFTLLFAVFDGKSMHSETKNSIMODRD	240
Db	181	VDLYKDLNSGLIGALLVCREGSLAKEKQTLAKFTLLFAVFDGKSMHSETKNSIMODRD	240
Qy	241	AASARAPKMTVNGVYNSLPGLICHRKSYVHWYIGMOTTEVHNSIFLBSGHTFLVRNH	300
Db	241	AASARAPKMTVNGVYNSLPGLICHRKSYVHWYIGMOTTEVHNSIFLBSGHTFLVRNH	300
Qy	301	ROASLEISPIFTFLAOTLLMDLGOFLLCCHISHQHDMGEAYKVYVSCPEEQOLAMKNE	360
Db	301	ROASLEISPIFTFLAOTLLMDLGOFLLCCHISHQHDMGEAYKVYVSCPEEQOLAMKNE	360
Qy	361	EAEYDDDLTDEMDVYRFPDDNSPFTQIRSVAKKRPKTWVHYIAAEEEDMDYAPLYLA	420
Db	361	EAEYDDDLTDEMDVYRFPDDNSPFTQIRSVAKKRPKTWVHYIAAEEEDMDYAPLYLA	420
Qy	421	PDORSYKSQYLNNGPQIRGKRYKRYRPMAYTDEFKTRALIOHESGILGPLLGYEGDTL	480
Db	421	PDORSYKSQYLNNGPQIRGKRYKRYRPMAYTDEFKTRALIOHESGILGPLLGYEGDTL	480
Qy	481	LIIFFKNOASRPYNIYPHGIDVAPLYSRRLPRGVKHLKDPILPBGIFKRYKWTYVEDCP	540
Db	481	LIIFFKNOASRPYNIYPHGIDVAPLYSRRLPRGVKHLKDPILPBGIFKRYKWTYVEDCP	540
Qy	541	TKSDPRCLTRYSSFFVMNERDLASGLIGPLLCIKESVQDORGNOIMSDRNYLIEVSDE	600
Db	541	TKSDPRCLTRYSSFFVMNERDLASGLIGPLLCIKESVQDORGNOIMSDRNYLIEVSDE	600
Qy	601	NRSWLTENIORFLPNAGVOLDPBPQASNMHSINGYVFDLSQVCLHVAWYTL	660
Db	601	NRSWLTENIORFLPNAGVOLDPBPQASNMHSINGYVFDLSQVCLHVAWYTL	660
Qy	661	IGAOTDPLSVFPGSYTRKHKMYEDTLLEPSSGETVPMSEMPGLMILGCHNSDFERNRG	720
Db	661	IGAOTDPLSVFPGSYTRKHKMYEDTLLEPSSGETVPMSEMPGLMILGCHNSDFERNRG	720
Qy	721	MTALLKVSQCKNTGDIYEDSYEDISAYLISKNNALIEPRSPSONSRHPTROKONATYI	780
Db	721	MTALLKVSQCKNTGDIYEDSYEDISAYLISKNNALIEPRSPSONSRHPTROKONATYI	780
Qy	781	PENDIEKTDPMFAHRTMPKIOVSSDDLMLLRQSPHPGLISLDOEAKYETESDDPS	840
Db	781	PENDIEKTDPMFAHRTMPKIOVSSDDLMLLRQSPHPGLISLDOEAKYETESDDPS	840
Qy	841	PGALDSNNSLSBMTHERPOLHSHGDMVTPPESGLOLRINEKLGTTAATELKLDFRVSST	900
Db	841	PGALDSNNSLSBMTHERPOLHSHGDMVTPPESGLOLRINEKLGTTAATELKLDFRVSST	900
Qy	901	SNMLISTIPSDNLAAGDNTSLSGSPSMVHNSQDLOTTLEFGKSSPFLRESGSPLSSEE	960
Db	901	SNMLISTIPSDNLAAGDNTSLSGSPSMVHNSQDLOTTLEFGKSSPFLRESGSPLSSEE	960
Qy	961	NNDKSLIESGLMNSOESMGKNVSTESGRLPKGRABGAPLLTKNALFKYISLAKTN	1020
Db	961	NNDKSLIESGLMNSOESMGKNVSTESGRLPKGRABGAPLLTKNALFKYISLAKTN	1020
Qy	1021	KTSNNSATNRKTHIDGFSLLIENSPSVWONILIESDTEFKKVTPLIDHRMLMDKNAATALRL	1080
Db	1021	KTSNNSATNRKTHIDGFSLLIENSPSVWONILIESDTEFKKVTPLIDHRMLMDKNAATALRL	1080
Qy	1081	NHMSNKTTSKKNMEVQOKKEGPIPPDAONPDMSPFKMLFLPESARWIORTHGKNSLSNG	1140
Db	1081	NHMSNKTTSKKNMEVQOKKEGPIPPDAONPDMSPFKMLFLPESARWIORTHGKNSLSNG	1140
Qy	1141	QGPSPKOLVSLGPEKSYBGONFLSEKNKYVVGKGFETKDVCLKEMVPPSSRNLFLTNIDN	1200
Db	1141	QGPSPKOLVSLGPEKSYBGONFLSEKNKYVVGKGFETKDVCLKEMVPPSSRNLFLTNIDN	1200

Qy	1201	LHENNTNOKKIOEIEIEKKTLLIOENVLPQIHYVTGKNFMKNLFLSTRONVBCSID	1260
Db	1201	LHENNTNOKKIOEIEIEKKTLLIOENVLPQIHYVTGKNFMKNLFLSTRONVBCSID	1260
Qy	1261	GAYAPVLODFRSLNDSTNRKTHAHFSKQKEENBLEGLGNOTKOIYEKVACTTRISPNT	1320
Db	1261	GAYAPVLODFRSLNDSTNRKTHAHFSKQKEENBLEGLGNOTKOIYEKVACTTRISPNT	1320
Qy	1321	SOONVTORSKRALQOFRLPEEPLEKRIIYDQTSQKMMKHLPPSTLOTIDNENE	1380
Db	1321	SOONVTORSKRALQOFRLPEEPLEKRIIYDQTSQKMMKHLPPSTLOTIDNENE	1380
Qy	1381	KGALTOSPLDCULTRSHSIPQANRSPRLIAKVSSPSPRIYTLRVLEFQDNSSHLPAAS	1440
Db	1381	KGALTOSPLDCULTRSHSIPQANRSPRLIAKVSSPSPRIYTLRVLEFQDNSSHLPAAS	1440
Qy	1441	RKDSGVQESSHFLQGAKKNNLSLILFLEMTGQDREVGSIGTSATNSVTYKKVENTVLP	1500
Db	1441	RKDSGVQESSHFLQGAKKNNLSLILFLEMTGQDREVGSIGTSATNSVTYKKVENTVLP	1500
Qy	1501	KPDLPKTSQVYELLPRVHYOKDLEPETSNGSPGHLDVBSGLQGTGEGAIKKNENARP	1560
Db	1501	KPDLPKTSQVYELLPRVHYOKDLEPETSNGSPGHLDVBSGLQGTGEGAIKKNENARP	1560
Qy	1561	GKVPFLVATNESSAKTPSKLIDPLAMDNNHYGTQIPKEMKSOEKSPERTAKKKOTLLSL	1620
Db	1561	GKVPFLVATNESSAKTPSKLIDPLAMDNNHYGTQIPKEMKSOEKSPERTAKKKOTLLSL	1620
Qy	1621	NACESNHAIAINEGONKPEIEVTNAKOGERTERLCSQNPVLRKHQREITRTTLOSQDEE	1680
Db	1621	NACESNHAIAINEGONKPEIEVTNAKOGERTERLCSQNPVLRKHQREITRTTLOSQDEE	1680
Qy	1681	IDYDPTISVEKKEDDPIYDDEBONSPPSPFKTRHYFTLAVERLMDYGMSSPHVLRNR	1740
Db	1681	IDYDPTISVEKKEDDPIYDDEBONSPPSPFKTRHYFTLAVERLMDYGMSSPHVLRNR	1740
Qy	1741	AOSGSVPQKVVYVQERTDOSTQPOLYKGBELNHLGLGYTAAEVEDIMATYTRNQASR	1800
Db	1741	AOSGSVPQKVVYVQERTDOSTQPOLYKGBELNHLGLGYTAAEVEDIMATYTRNQASR	1800
Qy	1801	PYSFYSLSIYEEBDOGAEPKRNKFNKNETKTFYVVOHHNAPTDEDFDCKAMAYFSDV	1860
Db	1801	PYSFYSLSIYEEBDOGAEPKRNKFNKNETKTFYVVOHHNAPTDEDFDCKAMAYFSDV	1860
Qy	1861	DLEKDVHSGILGRLVCHNTLIPAHGOVYVOBFALFTIIFDETKSWYFTENNERCRA	1920
Db	1861	DLEKDVHSGILGRLVCHNTLIPAHGOVYVOBFALFTIIFDETKSWYFTENNERCRA	1920
Qy	1921	PCNIOEDPTKENVYRPHAINGYIMDTLPGLVMAODORIMWYILSMGSVEMTHSHFSGH	1980
Db	1921	PCNIOEDPTKENVYRPHAINGYIMDTLPGLVMAODORIMWYILSMGSVEMTHSHFSGH	1980
Qy	1981	VFTYVRKKEEYKMAJLNYLPGVEFTEVEMLPKAGIMARVECLIGBHLNAGNSTLFLVSNKC	2040
Db	1981	VFTYVRKKEEYKMAJLNYLPGVEFTEVEMLPKAGIMARVECLIGBHLNAGNSTLFLVSNKC	2040
Qy	2041	QTPPLMASGHTRDFQITASQOGOMAPKLARLHYSGSINAMSTKEPFSYKVDLAPPII	2100
Db	2041	QTPPLMASGHTRDFQITASQOGOMAPKLARLHYSGSINAMSTKEPFSYKVDLAPPII	2100
Qy	2101	HGKTQGAOKFSSLYISOPTIYMSLSDKKQOTYRGNSTGLWFFGAVDSSGIKHNFEN	2160
Db	2101	HGKTQGAOKFSSLYISOPTIYMSLSDKKQOTYRGNSTGLWFFGAVDSSGIKHNFEN	2160
Qy	2161	PLIIRYIRLHPHYSTRSTLRMEIAGCDLNSCMPAGMESKASISDAQITTASVYTNMFA	2220
Db	2161	PLIIRYIRLHPHYSTRSTLRMEIAGCDLNSCMPAGMESKASISDAQITTASVYTNMFA	2220
Qy	2221	TWSPSKARLHLOGRSNARMROYVNNFEMLOYDPQTKYVGVYTGQVSKLSLTSWYVEFL	2280
Db	2221	TWSPSKARLHLOGRSNARMROYVNNFEMLOYDPQTKYVGVYTGQVSKLSLTSWYVEFL	2280

QY 2281 ISSSODGHQMTLFFQNGKVKVFGQNDSEFPVNSLDPPLTLRYLRHPQSMVHQIALRM 2340  
|||||  
Db 2281 ISSSODGHQMTLFFQNGKVKVFGQNDSEFPVNSLDPPLTLRYLRHPQSMVHQIALRM 2340  
|||||  
QY 2341 EYLGEAODPLY 2351  
|||||  
Db 2341 EYLGEAODPLY 2351  
|||||  
RESULT 24  
AAW11371  
ID AAW11371 standard; Protein; 2351 AA.  
AC AAW11371;  
XX 18-NOV-1997 (first entry)  
XX Active Factor VIII:C analogue N280X.  
XX  
KM Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;  
KM fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KM plasma protease; thrombin; immunogen; antibody; haemophilia; therapy;  
KM proteolytic cleavage.  
XX  
OS Homo sapiens.  
OS Synthetic.  
XX  
FH Key Location/Qualifiers  
FT Peptide 1..19  
FT /note= "signal peptide"  
FT Protein 20..2351  
FT /note= "mature Factor VIII:C"  
FT Region 20..1667  
FT /note= "heavy chain fragment"  
FT Modified-site 299  
FT /label= Phe, Glu, Pro  
FT Region 1668..2350  
FT /note= "light chain fragment"  
FT Domain 760..1667  
FT /note= "B domain"  
XX  
PN WC9703195-A1.  
XX  
PD 30-JAN-1997.  
XX  
PF 09-JUL-1996; 96WC-US11444.  
XX  
PR 11-JUL-1995; 95US-0001025.  
PA (CHIR ) CHIRON CORP.  
PI Cohen FE, Hung DT, Innis M;  
XX WPI; 1997-119050/11.  
XX  
PF Factor VIII:C analog modified adjacent to a non-activating Arg  
PF residue - used in the treatment of haemophiliacs, by improvement of  
PF haemostasis  
XX  
PS Claim 16: Page -: 90pp; English.  
XX  
CC AAW11330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments

CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophiliacs, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.

XX Sequence 2351 AA:

Query Match 99.98; Score 12411; DB 18; Length 2351;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2350; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 1 MQIELSTCFPLCLLRFCFSATRRYLGAVELSDMYQMSDLGELPYDAFPPRYKSPFN 60  
|||||  
Db 1 MQIELSTCFPLCLLRFCFSATRRYLGAVELSDMYQMSDLGELPYDAFPPRYKSPFN 60  
|||||  
QY 61 TSVYKKTLEFETDHLFNIARPRPMWGLLGPITGAELYDVVYTLKNMASHPSVLAHV 120  
|||||  
Db 61 TSVYKKTLEFETDHLFNIARPRPMWGLLGPITGAELYDVVYTLKNMASHPSVLAHV 120  
|||||  
QY 121 GVSYYKASSEGAEDDQTSQREKEDKYPGGSHTYYOYLKENGPMASDPLCLTYSLSH 180  
|||||  
Db 121 GVSYYKASSEGAEDDQTSQREKEDKYPGGSHTYYOYLKENGPMASDPLCLTYSLSH 180  
|||||  
QY 181 VDLVKDLSGLIGALLVCREGSLAKEKQTQLRKFILFVAFDEGKSWHSETKNSLMODRD 240  
|||||  
Db 181 VDLVKDLSGLIGALLVCREGSLAKEKQTQLRKFILFVAFDEGKSWHSETKNSLMODRD 240  
|||||  
QY 241 AASARAPKMTNGVNVNSRLPGLIGCRKSVYWHYIGTPEVHSFTLGGHFLYVRNH 300  
|||||  
Db 241 AASARAPKMTNGVNVNSRLPGLIGCRKSVYWHYIGTPEVHSFTLGGHFLYVRNH 300  
|||||  
QY 301 ROASLETSPTFLTAOTLMDLGOFLFCHSHOHDCBAYVYKSDCEPPEQLRMKNE 360  
|||||  
Db 301 ROASLETSPTFLTAOTLMDLGOFLFCHSHOHDCBAYVYKSDCEPPEQLRMKNE 360  
|||||  
QY 361 EAEYDDDLTDSMDVYRPPDDNSPFIQISYAKKHPRKTWHYVYIAAEEEDMDYAPLVYA 420  
|||||  
Db 361 EAEYDDDLTDSMDVYRPPDDNSPFIQISYAKKHPRKTWHYVYIAAEEEDMDYAPLVYA 420  
|||||  
QY 421 PDDSKSYOYLNNGPORIGRKKYKRPAYYDEFFKTRALIOHESGILPLLYGEVDTL 480  
|||||  
Db 421 PDDSKSYOYLNNGPORIGRKKYKRPAYYDEFFKTRALIOHESGILPLLYGEVDTL 480  
|||||  
QY 481 LIIFKNQASRPNIYPHGITDVRLPYLSRRLPKGVKHLKDPILLPEIFKRYKWTYVEDGP 540  
|||||  
Db 481 LIIFKNQASRPNIYPHGITDVRLPYLSRRLPKGVKHLKDPILLPEIFKRYKWTYVEDGP 540  
|||||  
QY 541 TKSDPRCLTRYSSPFVNMERDLASGLIGPLLICKEVDORNOQIMSKRNVILFSYFDE 600  
|||||  
Db 541 TKSDPRCLTRYSSPFVNMERDLASGLIGPLLICKEVDORNOQIMSKRNVILFSYFDE 600  
|||||  
QY 601 NRSWYLTENIQRFLPPAGVQLEDEEPQASIMHNSINGVPPSLQSLCLAEVAYWYIIS 660  
|||||  
Db 601 NRSWYLTENIQRFLPPAGVQLEDEEPQASIMHNSINGVPPSLQSLCLAEVAYWYIIS 660  
|||||  
QY 661 IGAOTDLSVFFSGYTFKKRVYEDTLTLFFPSGGEYFVSMENPGMLTLGCHNSDFNRNG 720  
|||||  
Db 661 IGAOTDLSVFFSGYTFKKRVYEDTLTLFFPSGGEYFVSMENPGMLTLGCHNSDFNRNG 720  
|||||  
QY 721 MVALIKYSCDKMTNGYEDSYEDISAVLSKNNALPPSPFSONSRHSTROKOFNATTI 780  
|||||  
Db 721 MVALIKYSCDKMTNGYEDSYEDISAVLSKNNALPPSPFSONSRHSTROKOFNATTI 780  
|||||  
QY 781 PENDEKTDPMFAHRPMKTONVSSDLMMLRQSTPHGISLSDLOEAKYEFSDPS 840  
|||||  
Db 781 PENDEKTDPMFAHRPMKTONVSSDLMMLRQSTPHGISLSDLOEAKYEFSDPS 840  
|||||  
QY 841 PAIDSNNSLSEMTHTFPOIHSQGMVTPPESGIOLRLNEKLGTTAATLKKDLDFKFSST 900  
|||||

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Db      841 PGALDSNNSISEMTHFRPOLHSGDNVFTPEESGLQRLNEKLGTTAATELKIDFVVSST 900
Qy      901 SNNLISTIPBDNLAAQTDNTSSLGCPSPMPVHYDSOLDTTLTGKSSPLTESSGSLSEB 960
Db      901 SNNLISTIPBDNLAAQTDNTSSLGCPSPMPVHYDSOLDTTLTGKSSPLTESSGSLSEB 960
Qy      961 NNDKLLSEGLMNSOESSMGKNVSTESGRLFPKGRAGHPALLTRPDNALFKVSIISLKTN 1020
Db      961 NNDKLLSEGLMNSOESSMGKNVSTESGRLFPKGRAGHPALLTRPDNALFKVSIISLKTN 1020
Qy      1021 KTSNNSATNKRKHGHPILLIENSPWOMLLESDPEFKYPLIHPRLMDKNATATL 1080
Db      1021 KTSNNSATNKRKHGHPILLIENSPWOMLLESDPEFKYPLIHPRLMDKNATATL 1080
Qy      1081 NMSNKTTSKKNMENVQOKKGGPIPPDAONPDMSFEKMLFPESARMIORTGKNSLNG 1140
Db      1081 NMSNKTTSKKNMENVQOKKGGPIPPDAONPDMSFEKMLFPESARMIORTGKNSLNG 1140
Qy      1141 QGSPKOLVSLGPEKSVESQNFLEKKNVVGKGEFTKDVGLKEWFPSSNLIPLTNLDN 1200
Db      1141 QGSPKOLVSLGPEKSVESQNFLEKKNVVGKGEFTKDVGLKEWFPSSNLIPLTNLDN 1200
Qy      1201 LHEHNTNOKKTOEIEKEKETLLOENVYLPOIHTVGTGNFKMLFLSTPQNVGSGYD 1260
Db      1201 LHEHNTNOKKTOEIEKEKETLLOENVYLPOIHTVGTGNFKMLFLSTPQNVGSGYD 1260
Qy      1261 GAVAPVLODFRSLNDSTNRTKKTAAHNSKGEENLEGLNGOTKOYVEKTACTRISPT 1320
Db      1261 GAVAPVLODFRSLNDSTNRTKKTAAHNSKGEENLEGLNGOTKOYVEKTACTRISPT 1320
Qy      1321 SQONFVTOBSKRALOKFLPLEETELERITIVDTSTONSKMKHLTPSTLTOIDYNEKE 1380
Db      1321 SQONFVTOBSKRALOKFLPLEETELERITIVDTSTONSKMKHLTPSTLTOIDYNEKE 1380
Qy      1381 KGAITOSPLSDCLTRSHSPQANSPLPIAKVSPFSIPYILTVLTVLPODNSSHLPAASY 1440
Db      1381 KGAITOSPLSDCLTRSHSPQANSPLPIAKVSPFSIPYILTVLTVLPODNSSHLPAASY 1440
Qy      1441 RKDSGVQESSHFLQAKAKNNLSLAILTLEMTGDQEVSLGTSATNSVYKKVENVYLP 1500
Db      1441 RKDSGVQESSHFLQAKAKNNLSLAILTLEMTGDQEVSLGTSATNSVYKKVENVYLP 1500
Qy      1501 KPDLPKTSKVELLPKVHAIYOKLFPETESNGSPGHLDEVESGLQTEGAIKMNEANRP 1560
Db      1501 KPDLPKTSKVELLPKVHAIYOKLFPETESNGSPGHLDEVESGLQTEGAIKMNEANRP 1560
Qy      1561 GAVPFLRVATESSAKTPSLDPLAMDNHGTQIPEEMKSOEKSEPEKTAKKKDITLSI 1620
Db      1561 GAVPFLRVATESSAKTPSLDPLAMDNHGTQIPEEMKSOEKSEPEKTAKKKDITLSI 1620
Qy      1621 NACESNHAIAINEGONKPEIYVMAKOGRTBERLCSQNPVYLRKHOREITITTLQSDOE 1680
Db      1621 NACESNHAIAINEGONKPEIYVMAKOGRTBERLCSQNPVYLRKHOREITITTLQSDOE 1680
Qy      1681 IDYDDTISVEMKKEFDIYDEDENOSPFSOKTRHYFIAAVERLMDYGSSSPHYLRN 1740
Db      1681 IDYDDTISVEMKKEFDIYDEDENOSPFSOKTRHYFIAAVERLMDYGSSSPHYLRN 1740
Qy      1741 AOSGSVPQFKVVOEFTDGSFTQPLYKGELEHNLGLPYIRAEVDNIWVTRNOASR 1800
Db      1741 AOSGSVPQFKVVOEFTDGSFTQPLYKGELEHNLGLPYIRAEVDNIWVTRNOASR 1800
Qy      1801 PYSFYSLSIYVEDDOGAEPKKNVYKPNKTYEFKVOHMAHPKDEFDCKAAVYSOV 1860
Db      1801 PYSFYSLSIYVEDDOGAEPKKNVYKPNKTYEFKVOHMAHPKDEFDCKAAVYSOV 1860
Qy      1861 DLEKDVHSGILGPLVCHTNTLNPAHGRQVTOEFALFTIFDETKSWYFENNERNCRA 1920
Db      1861 DLEKDVHSGILGPLVCHTNTLNPAHGRQVTOEFALFTIFDETKSWYFENNERNCRA 1920
Qy      1921 PCNTOMEDPTFKENYFPAHINCYIMDTLPGLVAAODRIWYLLMGSENHISIHSSGH 1980
Db      1921 PCNTOMEDPTFKENYFPAHINCYIMDTLPGLVAAODRIWYLLMGSENHISIHSSGH 1980

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Qy      1981 VFTVRRKEEYKALYNTLPGYFETVENLPSKAGIWRVBCILGEHLHNGHSTFLVYSNKC 2040
Db      1981 VFTVRRKEEYKALYNTLPGYFETVENLPSKAGIWRVBCILGEHLHNGHSTFLVYSNKC 2040
Qy      2041 QTPLGASGHIRDFQITASGOYGOMAPKLARLHYSGSINAMSTKEPWSIKYDLLAPMI 2100
Db      2041 QTPLGASGHIRDFQITASGOYGOMAPKLARLHYSGSINAMSTKEPWSIKYDLLAPMI 2100
Qy      2101 HGKRTGARGKSSLYTISQFTIYNSLDGCKKQTYRGNSTGTLWYFGVNDVSGIKHNIFN 2160
Db      2101 HGKRTGARGKSSLYTISQFTIYNSLDGCKKQTYRGNSTGTLWYFGVNDVSGIKHNIFN 2160
Qy      2161 PPIIARIYLPHTHYSINSTRLMEKWCGLNSCSPRLMESKALSDAQITASSYTNMFA 2220
Db      2161 PPIIARIYLPHTHYSINSTRLMEKWCGLNSCSPRLMESKALSDAQITASSYTNMFA 2220
Qy      2221 TWSPSKARLHLQGRSNAMRPQVNNPKEMLOVDFOKTMKVTGVTTOGVKSLTSMYKFEI 2280
Db      2221 TWSPSKARLHLQGRSNAMRPQVNNPKEMLOVDFOKTMKVTGVTTOGVKSLTSMYKFEI 2280
Qy      2281 ISSSODGHQMTLFPQNGKVKYFGQNDPSFTPVVNSLDPLLTRYLRIHPQSWHQAIALRM 2340
Db      2281 ISSSODGHQMTLFPQNGKVKYFGQNDPSFTPVVNSLDPLLTRYLRIHPQSWHQAIALRM 2340
Qy      2341 EYLGCENODLY 2351
Db      2341 EYLGCENODLY 2351

RESULT 25
AA00465
ID AA00465 standard; Protein; 2351 AA.
AC AA00465;
DT 19-SEP-1996 (first entry)
DE Factor-VIII.
DX
XX Factor-VIII.
XX Factor-VIII; retrovirus; vector; haemophilia A; gene therapy.
XX Homo sapiens.
XX
XX Key
XX Peptide 1..19
XX FT /label= Sig_peptide
XX FT 20..2351
XX FT Protein /label= Mat_protein
XX
XX W09621035-A2.
XX PD 11-JUL-1996.
XX PF 18-DEC-1995; 95MO-US16582.
XX PR 30-DEC-1994; 94US-0366851.
XX PA (CHIR ) CHIRON VIAGENE INC.
XX PI Bodner M, Chang S, Chi-Tang Hsu D, De Polo NJ;
XX DR WPI: 1996-336010/33.
XX DR N-PSDB; AAT31031.
XX PT Retroviral vector directing expression of full length factor VIII -
XX PS used in the gene therapy and treatment of haemophilia A
XX PS Disclosure: Page 69-75; 86pp; English.
XX
XX A full-length cDNA clone (AAT31031) codes for human Factor-VIII
XX CC (AA00465), a trace plasma glycoprotein which acts as a cofactor in
XX CC conjunction with Factor-IXa in the activation of Factor-X.

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CC Retroviral vectors comprising the full-length cDNA can be efficiently  
CC packaged into infectious retroviral particles. These may be used to  
CC transduce cells either in vivo or ex vivo. Factor-VIII expressed  
CC from such transduced cells will be processed and transported in a  
CC fashion analogous to the expression product of a normal Factor-VIII  
CC gene. Retroviral particles harbouring such vectors will be useful  
CC in the gene therapy of haemophilia A.

XX Sequence 2351 AA:

Query Match 99.9%; Score 12409; DB 17; Length 2351;

Best Local Similarity 100.0%; Pred. No. 0;

Matches 2150; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY	1	MOELSTCFELCLRFCSATRRYYLGAVELSMYQMSDLGELPVDARPPRPYKSFPPN	60
DB	1	MOELSTCFELCLRFCSATRRYYLGAVELSMYQMSDLGELPVDARPPRPYKSFPPN	60
QY	61	TSVYKKTLFEVPTDHLFNIAKPRPMGLGPTOAEYDTVYTLKMAHPVSLHAY	120
DB	61	TSVYKKTLFEVPTDHLFNIAKPRPMGLGPTOAEYDTVYTLKMAHPVSLHAY	120
QY	121	GVSTWAKSEGAEXDQTSQREKEDKVPFGSHYVWQYLAENGPMASDPLCLTYSYLSH	180
DB	121	GVSTWAKSEGAEXDQTSQREKEDKVPFGSHYVWQYLAENGPMASDPLCLTYSYLSH	180
QY	181	VDLVKDLNSGLIGALLVREGSLAKETQTLHKFILLFAVDEGSMHSETKNSLMQDD	240
DB	181	VDLVKDLNSGLIGALLVREGSLAKETQTLHKFILLFAVDEGSMHSETKNSLMQDD	240
QY	241	AASARAPKMHVNYGVNRSPLGLIGHKRSYVWHYIGMTTPRYHSLFDEGTFYLRNH	300
DB	241	AASARAPKMHVNYGVNRSPLGLIGHKRSYVWHYIGMTTPRYHSLFDEGTFYLRNH	300
QY	301	FOASBSSDITTELTAQTLMDLGOFLLFCHSISSHQDGMAYVAVKDSCEPEOLRKNNE	360
DB	301	FOASBSSDITTELTAQTLMDLGOFLLFCHSISSHQDGMAYVAVKDSCEPEOLRKNNE	360
QY	361	EAEYDDDLTDSBMDVYRFDDDNSPFTQIRYAKKHPTWVHYTAAEEDMDYAPLVLA	420
DB	361	EAEYDDDLTDSBMDVYRFDDDNSPFTQIRYAKKHPTWVHYTAAEEDMDYAPLVLA	420
QY	421	PDDRSTYSOYLNNNGPQIRGRKKYKVRMATYDTEFTRAIQHEBSGLIGLAGEVDL	480
DB	421	PDDRSTYSOYLNNNGPQIRGRKKYKVRMATYDTEFTRAIQHEBSGLIGLAGEVDL	480
QY	481	LIIFKNQASRPYNIYPHGITDVRPLYSRLLPKGVKHLKDFLLPGLPFKYKMYTVYEDGP	540
DB	481	LIIFKNQASRPYNIYPHGITDVRPLYSRLLPKGVKHLKDFLLPGLPFKYKMYTVYEDGP	540
QY	541	TKSDPRCLTRYYSFVNNMRDLASGLIGPLLIYKESVDORGNQIMSDKRVLLFSVDE	600
DB	541	TKSDPRCLTRYYSFVNNMRDLASGLIGPLLIYKESVDORGNQIMSDKRVLLFSVDE	600
QY	601	NRSWYLTENIORFLPMPAGVQLEDEPFOASNIWHSINGVYPSIOLASCLHEVAWYVILS	660
DB	601	NRSWYLTENIORFLPMPAGVQLEDEPFOASNIWHSINGVYPSIOLASCLHEVAWYVILS	660
QY	661	IGAOTDFLSVFSFGYTFKHKVYEDTLTLFPFSGETVFMSENPGLWILGCHNSDFRNG	720
DB	661	IGAOTDFLSVFSFGYTFKHKVYEDTLTLFPFSGETVFMSENPGLWILGCHNSDFRNG	720
QY	721	MTALLKVSCKDKWGTGYEDSEDIASVLLSKNNAIEPSPFONSRRHSTROKOFANNTI	780
DB	721	MTALLKVSCKDKWGTGYEDSEDIASVLLSKNNAIEPSPFONSRRHSTROKOFANNTI	780
QY	781	PENDIEKTDPMFAHRTPMKTIQNVSSDLMLLROSPTPHGISLSDLOEAYEFESDDPS	840
DB	781	PENDIEKTDPMFAHRTPMKTIQNVSSDLMLLROSPTPHGISLSDLOEAYEFESDDPS	840
QY	841	PGAIDSNNSLSEWTHRPOQLHHSQDMVFTPESSLOLRNEKIGTAAATELKLDIFYVST	900
DB	841	PGAIDSNNSLSEWTHRPOQLHHSQDMVFTPESSLOLRNEKIGTAAATELKLDIFYVST	900

QY	901	NNNLIPTSPDNLAAAGTDNNTSLGSPSPMVHYDSQLDITLFGKSSPLTESGPLSLEE	960
DB	901	NNNLIPTSPDNLAAAGTDNNTSLGSPSPMVHYDSQLDITLFGKSSPLTESGPLSLEE	960
QY	961	NNSKILLESGLMNSQESGKKNYSFRESGRFLKGRARAPALLFKDAPLKYVLSILKTN	1020
DB	961	NNSKILLESGLMNSQESGKKNYSFRESGRFLKGRARAPALLFKDAPLKYVLSILKTN	1020
QY	1021	KTSNNSATNRKTHIDGSPSLIENSPPYQNNLESOTERKKTPLIHDRMLMDKNTALRL	1080
DB	1021	KTSNNSATNRKTHIDGSPSLIENSPPYQNNLESOTERKKTPLIHDRMLMDKNTALRL	1080
QY	1081	NHMSNKTYSKKNMEVQCKEGPITPDPAQNPDMSPFKMLFLPESARWIOPTHGKNSLNG	1140
DB	1081	NHMSNKTYSKKNMEVQCKEGPITPDPAQNPDMSPFKMLFLPESARWIOPTHGKNSLNG	1140
QY	1141	QGPSPKQVSLGPEKSVGONFLSEKKKVVYVKGFEFTDVLKEMVPPSSRNLFUNLDN	1200
DB	1141	QGPSPKQVSLGPEKSVGONFLSEKKKVVYVKGFEFTDVLKEMVPPSSRNLFUNLDN	1200
QY	1201	LHENTHNOEKIODEIEKKETTLIOENVVLPQIHYTGTKFPMNLFLSTRQNBGSYD	1260
DB	1201	LHENTHNOEKIODEIEKKETTLIOENVVLPQIHYTGTKFPMNLFLSTRQNBGSYD	1260
QY	1261	GAYAPVLODFRSLNDSTNRKTHAHSKKGEENLEGLNQTOIYEKYACTTRISPWT	1320
DB	1261	GAYAPVLODFRSLNDSTNRKTHAHSKKGEENLEGLNQTOIYEKYACTTRISPWT	1320
QY	1321	SOONFYTORSKRALQOPFLPEFELEKRTIYDDPTSTQMSKNMHLPSLTQIDVNEKE	1380
DB	1321	SOONFYTORSKRALQOPFLPEFELEKRTIYDDPTSTQMSKNMHLPSLTQIDVNEKE	1380
QY	1381	KGATISPLSDCLTSHSTPOANSPLPLAKYSFSPSTPIYTLRVLPQONSHLPPAASY	1440
DB	1381	KGATISPLSDCLTSHSTPOANSPLPLAKYSFSPSTPIYTLRVLPQONSHLPPAASY	1440
QY	1441	RKRDGVOESSHFLOGAKKNNLSLITLLEMTGDORREVSGLSGTSATNSVTYKVENTYLP	1500
DB	1441	RKRDGVOESSHFLOGAKKNNLSLITLLEMTGDORREVSGLSGTSATNSVTYKVENTYLP	1500
QY	1501	KPDLPTKSGVELLKRVYIYOKDFFETNSGPGHLDIVGSSLLQSTEGAIKWNANRP	1560
DB	1501	KPDLPTKSGVELLKRVYIYOKDFFETNSGPGHLDIVGSSLLQSTEGAIKWNANRP	1560
QY	1561	GKYPFLKATSESSATTPSKLLDPLAMNHTGQIIPREEMKGOEKSPEKTAFFKKOTIISL	1620
DB	1561	GKYPFLKATSESSATTPSKLLDPLAMNHTGQIIPREEMKGOEKSPEKTAFFKKOTIISL	1620
QY	1621	NACESNHATAINEGONRPELEVMAKQTERLCSQNPVYLKHOBEITRTLOSDOE	1680
DB	1621	NACESNHATAINEGONRPELEVMAKQTERLCSQNPVYLKHOBEITRTLOSDOE	1680
QY	1681	IDYDDTISYEMKKEPDFIYDDEDNQSPRSFOKTRHYFLAVERLMQYGMSSPHYLNR	1740
DB	1681	IDYDDTISYEMKKEPDFIYDDEDNQSPRSFOKTRHYFLAVERLMQYGMSSPHYLNR	1740
QY	1741	AQSGSVQKRYVFOEPLDGSFTQPLRGGLNHLGLGPTIRAEVEDNIMTFERRQAR	1800
DB	1741	AQSGSVQKRYVFOEPLDGSFTQPLRGGLNHLGLGPTIRAEVEDNIMTFERRQAR	1800
QY	1801	PYSFYSLSIYSEEDROGAEPKRFVAPNPTKTYEKVYQNHMAPTKDEFCAMAYFSOV	1860
DB	1801	PYSFYSLSIYSEEDROGAEPKRFVAPNPTKTYEKVYQNHMAPTKDEFCAMAYFSOV	1860
QY	1861	DLEKDVHSGLIGPLLVCTNTNLNANROVTOQERLFTTJDETKSMYTFEMENRCRA	1920
DB	1861	DLEKDVHSGLIGPLLVCTNTNLNANROVTOQERLFTTJDETKSMYTFEMENRCRA	1920
QY	1921	PCNTOMEDPTFEKENTRFAINGYIMDTLPGLVMAODORIIMYLLSMGSENHISIHFSGH	1980
DB	1921	PCNTOMEDPTFEKENTRFAINGYIMDTLPGLVMAODORIIMYLLSMGSENHISIHFSGH	1980



Dh 541 TRSDPRCLTRYSSFEVNMERDLASGLIGPLLCYKESVDORGNQIMSDKRNVLIFSVPDE 600  
QY 601 NRSWYLTENIOFPLPNPAGVOLJEDPEFOASNIHMSINGVDSLOLSVCLHEVAWYIIS 660  
Dh 602 NRSWYLTENIORPLPNPAGVOLJEDPEFOASNIHMSINGVDSLOLSVCLHEVAWYIIS 660  
QY 661 IGAOTDPLSVFSGYTFKHKMYVEDTLTLPFSGEFTVEMSMENGCIATIGCHNSDFRNG 720  
Dh 661 IGAOTDPLSVFSGYTFKHKMYVEDTLTLPFSGEFTVEMSMENGCIATIGCHNSDFRNG 720  
QY 721 MTALLKVSQCDKNTGDYTEDSYEDISAYLLSKNNALEPRSESQNSRHPSTRQORFNAATTI 780  
Dh 721 MTALLKVSQCDKNTGDYTEDSYEDISAYLLSKNNALEPRSESQNSRHPSTRQORFNAATTI 780  
QY 781 PENDIEKTOPWFARHCTPMPKIQNVSSSDLLMLRQSPRHGSLSDLOEAKYEFEDDPS 840  
Dh 781 PENDIEKTOPWFARHCTPMPKIQNVSSSDLLMLRQSPRHGSLSDLOEAKYEFEDDPS 840  
QY 841 PGALDSNNLSLEMTFRRPOLHSGDMVTPESGLQRLNEMKLGTAATLKLDFKVSST 900  
Dh 841 PGALDSNNLSLEMTFRRPOLHSGDMVTPESGLQRLNEMKLGTAATLKLDFKVSST 900  
QY 901 SNNLITIPSDNLAAGTNTSSLCGPPSMVHYDSQDLTTLFEGKSSPLTESGGPLSLEE 960  
Dh 901 SNNLITIPSDNLAAGTNTSSLCGPPSMVHYDSQDLTTLFEGKSSPLTESGGPLSLEE 960  
QY 961 NNDKLESGLMNSQESSMGKNVSTESGRLFGKRAHGPALLTKDNALFKVSIISLKTN 1020  
Dh 961 NNDKLESGLMNSQESSMGKNVSTESGRLFGKRAHGPALLTKDNALFKVSIISLKTN 1020  
QY 1021 KTSNNSATNRKTHIGPILLSLENSPYWONILSDTEFKKVTPLIHDMLMDKNATALLR 1080  
Dh 1021 KTSNNSATNRKTHIGPILLSLENSPYWONILSDTEFKKVTPLIHDMLMDKNATALLR 1080  
QY 1081 NMSNKTSSKNMENVQOKKEGPIPPDAONPDMSFFKMLFPESARWIORHGNISLNG 1140  
Dh 1081 NMSNKTSSKNMENVQOKKEGPIPPDAONPDMSFFKMLFPESARWIORHGNISLNG 1140  
QY 1141 QGSPKQVLSLGPESKSVESQNFLESEKRVVVGGEFTKDVGLKEWVFPSSRNLEFLNLDN 1200  
Dh 1141 QGSPKQVLSLGPESKSVESQNFLESEKRVVVGGEFTKDVGLKEWVFPSSRNLEFLNLDN 1200  
QY 1201 LHENNTNDEKKTIOEIEKKEFTLQENNVLPOLHTVTGKNMKMLPLSTRONVGSVD 1260  
Dh 1201 LHENNTNDEKKTIOEIEKKEFTLQENNVLPOLHTVTGKNMKMLPLSTRONVGSVD 1260  
QY 1261 GAVAPVLODFRSLINDSTNRTKKAHFSKKGEBENLEGLGNQTOIYEKYACTTRISPM 1320  
Dh 1261 GAVAPVLODFRSLINDSTNRTKKAHFSKKGEBENLEGLGNQTOIYEKYACTTRISPM 1320  
QY 1321 SQONFTVORSKRALQOFRLPEETELEKRIIVDTSTQSKNMKHLPPSTLTQIDYNEKE 1380  
Dh 1321 SQONFTVORSKRALQOFRLPEETELEKRIIVDTSTQSKNMKHLPPSTLTQIDYNEKE 1380  
QY 1381 KGATQSPSLSDCLTRHSHIPOANSPLPIAKVSSFSIRPYLTUVLPFONSSHLPAASY 1440  
Dh 1381 KGATQSPSLSDCLTRHSHIPOANSPLPIAKVSSFSIRPYLTUVLPFONSSHLPAASY 1440  
QY 1441 RKKDSVOESSHFLQAKKNNLSLAILLTLEMTSDOREVSGLSGTSATNSVYTKRVENVTL 1500  
Dh 1441 RKKDSVOESSHFLQAKKNNLSLAILLTLEMTSDOREVSGLSGTSATNSVYTKRVENVTL 1500  
QY 1501 KPDLPTSGKVELLPVHYHOKDLFPTETSGNSPGLDIVEGSLLOGEGAIKKNENRNP 1560  
Dh 1501 KPDLPTSGKVELLPVHYHOKDLFPTETSGNSPGLDIVEGSLLOGEGAIKKNENRNP 1560  
QY 1561 GKVPFLKATESSAKTPSKLDPLAMDNHYGTOIPKEEKSOEKSPEKTAFFKKDITLIS 1620  
Dh 1561 GKVPFLKATESSAKTPSKLDPLAMDNHYGTOIPKEEKSOEKSPEKTAFFKKDITLIS 1620  
QY 1621 NACESNHAIAINEGONREIEVTWAKOGRTERLCSQNPVYLKROREITRTTLOSQOE 1680  
Dh 1621 NACESNHAIAINEGONREIEVTWAKOGRTERLCSQNPVYLKROREITRTTLOSQOE 1680

QY 1681 IDYDDTISYEMKKEDEFDIYDEDENOSPRSFORKTRHYEIAAVERLMDYGMSSPHYLNR 1740  
Dh 1681 IDYDDTISYEMKKEDEFDIYDEDENOSPRSFORKTRHYEIAAVERLMDYGMSSPHYLNR 1740  
QY 1741 AOGSGVPOFKKVVPOEFTDGSFTQPOLRGELNENHGLGPIYIAAEVENDIMVTFRNOASR 1800  
Dh 1741 AOGSGVPOFKKVVPOEFTDGSFTQPOLRGELNENHGLGPIYIAAEVENDIMVTFRNOASR 1800  
QY 1801 PYSFYSSLSIYEDDROGAEPKRVKVPNETKITTYWKQHHMATKROEFCCKMAAFSDV 1860  
Dh 1801 PYSFYSSLSIYEDDROGAEPKRVKVPNETKITTYWKQHHMATKROEFCCKMAAFSDV 1860  
QY 1861 DLEKDVHSGILGPLVCHTNTLNPAGROVYQOEFALFFTJEDETKSMYTEMMERNCA 1920  
Dh 1861 DLEKDVHSGILGPLVCHTNTLNPAGROVYQOEFALFFTJEDETKSMYTEMMERNCA 1920  
QY 1921 PCNTOMEDPTFKENTRFAHNGYIMDTLPGLVYAADORIRMYLLSMGSNENIHSIHFSCH 1980  
Dh 1921 PCNTOMEDPTFKENTRFAHNGYIMDTLPGLVYAADORIRMYLLSMGSNENIHSIHFSCH 1980  
QY 1981 VFTYRKKEEYKALYNLYPGYFETVEKLPKAGIWRVCEIIGELHAGMSTLPVYSNKC 2040  
Dh 1981 VFTYRKKEEYKALYNLYPGYFETVEKLPKAGIWRVCEIIGELHAGMSTLPVYSNKC 2040  
QY 2041 QTPLGNASGHINDFOITASGOYGOMAPKLARLHYSGSINAMSTKEPFSWIKVDLAPMII 2100  
Dh 2041 QTPLGNASGHINDFOITASGOYGOMAPKLARLHYSGSINAMSTKEPFSWIKVDLAPMII 2100  
QY 2101 HGIKTGOAGOKFSSLYISQFIIMSLDGKKMOTYKRNSTGTLMVFGNVDSGIRKINIFN 2160  
Dh 2101 HGIKTGOAGOKFSSLYISQFIIMSLDGKKMOTYKRNSTGTLMVFGNVDSGIRKINIFN 2160  
QY 2161 PPIIARIIRLHPTHYISITSTIRMLMCCDLNCSMPIGESKAIISDQIATASSYFTNMFA 2220  
Dh 2161 PPIIARIIRLHPTHYISITSTIRMLMCCDLNCSMPIGESKAIISDQIATASSYFTNMFA 2220  
QY 2221 TWSPSKARLHLOGRSNANRPQVNNPKEMLOVDFOKTMKVYGVTTQGVKSLLTSMYKEFL 2280  
Dh 2221 TWSPSKARLHLOGRSNANRPQVNNPKEMLOVDFOKTMKVYGVTTQGVKSLLTSMYKEFL 2280  
QY 2281 ISSSQDGHOMTLFPONGVYKVFQGNODSFPPVYNSLDPLLTRYLRIHPQSWYHOALRPM 2340  
Dh 2281 ISSSQDGHOMTLFPONGVYKVFQGNODSFPPVYNSLDPLLTRYLRIHPQSWYHOALRPM 2340  
QY 2341 EVLGCEADOLY 2351  
Dh 2341 EVLGCEADOLY 2351  
RESULT 27  
AAB48843  
ID AAB48843 standard; protein: 2351 AA.  
XX  
AC AAB48843;  
XX  
DE Human factor VIII, SEQ ID NO:2.  
XX  
DT 13-MAR-2001 (first entry)  
XX  
KW Factor VIII: human; A2 domain; C2 domain; LRP-mediated plasma clearance;  
KW receptor-dependent clearance; receptor-independent clearance;  
KW haemophilia; half-life.  
XX  
OS Homo sapiens.  
XX  
PN WO20007174-A2.  
XX  
PD 30-NOV-2000.  
XX  
PF 24-MAY-2000; 2000WO-US14111.  
XX  
PR 24-MAY-1999; 99US-0135847.



XX	(AMNA-) AMERICAN NAT RED CROSS.	
PA		
XX		
PI	Saenko EL, Strickland DK;	
XX		
DR	WPI: 2001-025163/03.	
DR	N-PSDB: AAC87526.	
XX		
PT	Factor VIII mutants having increased half-life useful for treating	
PT	hemophilia, comprise one or more amino acid substitutions in the A2	
PT	and/or C2 domain of factor VIII	
XX		
PS	Disclosure; Fig 3A-B; 121pp; English.	
XX		
CC	The invention relates to human factor VIII mutants comprising an amino	
CC	acid substitution at one or more positions in the A2 domain and/or an	
CC	amino acid substitution at one or more positions in the C2 domain.	
CC	The invention also encompasses a factor VIII mutant which lacks a B	
CC	domain (AAB48842). The factor VIII mutants have an increased half-life	
CC	in the bloodstream. The A2 domain mutants exhibit reduced LRP-dependent	
CC	(receptor-dependent) clearance of factor VIII, while C2 domain mutants	
CC	have reduced receptor-independent clearance. The invention also relates	
CC	to a method of using RAP (receptor associated protein), a protein which	
CC	inhibits LRP (low density lipoprotein related protein)-mediated ligand	
CC	internalisation, to increase the half-life of factor VIII. The mutant	
CC	factor VIII proteins, and nucleotides encoding them, are useful	
CC	for treating haemophilia. RAP, LRP-binding RAP mutants or fragments, and	
CC	nucleic acids encoding them may also be used in the treatment of	
CC	haemophilia. In combination with a mutant factor VIII protein or DNA of	
CC	the invention. The invention provides means of increasing the half-life	
CC	of factor VIII by reducing its clearance from plasma. The present	
CC	sequence represents human factor VIII.	
CC		
SQ	Sequence 2351 AA:	
Query Match	99.9%; Score 12409; DB 22; Length 2351;	
Best Local Similarity	100.0%; Pred. No. 0;	
Matches 2350; Conservative	0; Mismatches 1; Indels 0; Gaps 0;	
QY	1	1
DB	1	1
QY	61	61
DB	61	61
QY	121	121
DB	121	121
QY	181	181
DB	181	181
QY	241	241
DB	241	241
QY	301	301
DB	301	301
QY	361	361
DB	361	361
QY	421	421
DB	421	421
QY	481	481
DB	481	481
QY	540	540
DB	540	540
QY	600	600
DB	600	600
QY	660	660
DB	660	660
QY	720	720
DB	720	720
QY	780	780
DB	780	780
QY	840	840
DB	840	840
QY	900	900
DB	900	900
QY	960	960
DB	960	960
QY	1020	1020
DB	1020	1020
QY	1080	1080
DB	1080	1080
QY	1140	1140
DB	1140	1140
QY	1200	1200
DB	1200	1200
QY	1260	1260
DB	1260	1260
QY	1320	1320
DB	1320	1320
QY	1380	1380
DB	1380	1380
QY	1440	1440
DB	1440	1440
QY	1500	1500
DB	1500	1500
QY	1560	1560
DB	1560	1560
QY	1620	1620
DB	1620	1620

QY	1621	NACSNHAIATAINEGONKPEIEVTWAKOGTERLCSQNPVYLKROHREITRTTLOSDEE	1680
Db	1621	NACSNHAIATAINEGONKPEIEVTWAKOGTERLCSQNPVYLKROHREITRTTLOSDEE	1680
QY	1681	IDYDDTSVEMKKEPDYDEDENSPRSPQKTRHYFAAVERIMPMYGMSSPHYLRR	1740
Db	1681	IDYDDTSVEMKKEPDYDEDENSPRSPQKTRHYFAAVERIMPMYGMSSPHYLRR	1740
QY	1741	AQSGSVPOKRYVFOEFTDGSFTOPLYRGELNHGLGAPTRAEVDNIMVTFERNQASR	1800
Db	1741	AQSGSVPOKRYVFOEFTDGSFTOPLYRGELNHGLGAPTRAEVDNIMVTFERNQASR	1800
QY	1801	PYSFYSLSISEDDROGAEBRNKFNVPNETKTYEMKVOHMAPTKDEFDCKAMAFESDV	1860
Db	1801	PYSFYSLSISEDDROGAEBRNKFNVPNETKTYEMKVOHMAPTKDEFDCKAMAFESDV	1860
QY	1861	DLEKDVHSGILGIPLVCHNTNLNPAHROYVQGEALFTTLEDETKSMYETENNERCRA	1920
Db	1861	DLEKDVHSGILGIPLVCHNTNLNPAHROYVQGEALFTTLEDETKSMYETENNERCRA	1920
QY	1921	PCNIQMEDPTFKENYRFAHNGYIMDTLPGLVMAODQRIRWYLLSMGSNNIHSIHFSCH	1980
Db	1921	PCNIQMEDPTFKENYRFAHNGYIMDTLPGLVMAODQRIRWYLLSMGSNNIHSIHFSCH	1980
QY	1981	VFTYRKKEEKKALYNLPGVFETVEMLPKAGIMVECLIGEHLHAGMSTLEFLVYSNKC	2040
Db	1981	VFTYRKKEEKKALYNLPGVFETVEMLPKAGIMVECLIGEHLHAGMSTLEFLVYSNKC	2040
QY	2041	OTPLGMAHGIRDPQITASGOYGOMAKLARKLHSSISINASTKEPSPWIKVLLAPMII	2100
Db	2041	OTPLGMAHGIRDPQITASGOYGOMAKLARKLHSSISINASTKEPSPWIKVLLAPMII	2100
QY	2101	HGIKTQGAQKFSLSYISQFTIMTSLDGKKWQTYRGNSTGTLMPFGNVDSGKIKINIFN	2160
Db	2101	HGIKTQGAQKFSLSYISQFTIMTSLDGKKWQTYRGNSTGTLMPFGNVDSGKIKINIFN	2160
QY	2161	PLIARIYIRLHPHYISIRSTRLMELMCGDNCNSMPLGMESKATSDAQITASSYFTNMFA	2220
Db	2161	PLIARIYIRLHPHYISIRSTRLMELMCGDNCNSMPLGMESKATSDAQITASSYFTNMFA	2220
QY	2221	TWSPSKARLHLOGRBNARPOVNNPKEMLOYDOKIMKYTGVTQGVKSLTSMYKEL	2280
Db	2221	TWSPSKARLHLOGRBNARPOVNNPKEMLOYDOKIMKYTGVTQGVKSLTSMYKEL	2280
QY	2281	ISSSQDGHOWTLFPONGKVKVFGCNDSFTPVVNSIDPPLIRYLRIHPOSWVHOIALRM	2340
Db	2281	ISSSQDGHOWTLFPONGKVKVFGCNDSFTPVVNSIDPPLIRYLRIHPOSWVHOIALRM	2340
QY	2341	EVLGCEADODLY 2351	
Db	2341	EVLGCEADODLY 2351	

## RESULT 28

AAW11399 standard; Protein; 2351 AA.

ID	AAW11399	standard; Protein; 2351 AA.
AC	AAW11399;	
DT	18-NOV-1997	(first entry)
DE	Active Factor VIII:C analogue, delta 748, + residue 748 insertion.	
XX		
XX	Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;	
KM	fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;	
KM	plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;	
KM	proteolytic cleavage.	
XX		
OS	Homo sapiens.	
XX		
OS	Synthetic.	
XX		
FH	Key	Location/Qualifiers

FT	Peptide	1..19
FT	/note= "signal peptide"	
FT	Protein	20..2351
FT	/note= "mature Factor VIII:C"	
FT	Region	20..1667
FT	/note= "heavy chain fragment"	
FT	Misc-difference	766..767
FT	/note= "site of 1 residue deletion"	
FT	Modified-site	767
FT	/note= "inserted residue, optionally deleted"	
FT	Region	1668..2350
FT	/note= "light chain fragment"	
FT	Domain	760..1667
FT	/note= "B domain"	
XX		
PD	WO9703195-A1.	
XX		
XX	30-JAN-1997.	
PF	09-JUL-1996; 96WO-0511444.	
XX		
PR	11-JUL-1995; 95DS-0001025.	
XX		
PA	(CHIR ) CHIRON CORP.	
XX		
PI	Cohen FE, Hung DF, Innis M;	
XX		
DR	WPI: 1997-119050/11.	
XX		
PT	Factor VIII:C analog modified adjacent to a non-activating Arg	
PT	residue - used in the treatment of haemophilias, by improvement of	
PT	haemostasis	
XX		
PS	Claim 23; Page -; 90pp; English.	
XX		
CC	AAW11330-W11472 represent active Factor VIII:C analogues of the	
CC	invention. These sequences were created by mutating the wild type Factor	
CC	VIII:C coding sequence (see AAT51357) using mutagenic primers. The	
CC	analogues comprise a native Factor VIII:C polypeptide modified at a site	
CC	adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg	
CC	dipeptide is created. Factor VIII:C is a large glycoprotein that	
CC	participates in the blood coagulation cascade that ultimately converts	
CC	soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A	
CC	deficiency in Factor VIII:C is responsible for haemophilia A, which is an	
CC	X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is	
CC	activated by plasma proteases, such as thrombin. During activation the	
CC	mature polypeptide is cleaved to generate heavy and light chain fragments	
CC	that are further cleaved. Complexes of two or more of the analogues,	
CC	nucleic acids and vectors encoding them may be used alone or in	
CC	conjunction with each other, for the prevention or treatment of active	
CC	Factor VIII:C deficiency in a mammal. The analogues may be used as	
CC	immunogens to raise antibodies, and in the treatment of haemophilias, by	
CC	improvement of haemostasis. The analogues are resistant to proteolytic	
CC	cleavage and display increased plasma half-life. They may be administered	
CC	at lower dosages and by different modes of administration.	
XX		
SQ	Sequence	2351 AA:
	Query Match	99.9%; Score 12408; DB 18; Length 2351;
	Best Local Similarity	100.0%; Pred. No. 0;
	Matches 2350; Conservative	0; Mismatches . 1; Indels 0; Gaps 0;
QY	1	MOLELSTCFPLCLARFCPSATRRYLGAVELSMQYMOSSDLGELPVARPPRPVPSPPFN 60
Db	1	MOLELSTCFPLCLARFCPSATRRYLGAVELSMQYMOSSDLGELPVARPPRPVPSPPFN 60
QY	61	TSVYVYKTLFVEFTDHLFENAKRPPRMGLLQPTQAEVDTYVYITLKMAASHPSLAV 120
Db	61	TSVYVYKTLFVEFTDHLFENAKRPPRMGLLQPTQAEVDTYVYITLKMAASHPSLAV 120
QY	121	GVSYWKASGAEYDDOTSOREKEDDVFPGSGHTVWQVLEKNCPNAPSPLCLTYSYLSH 180
Db	121	GVSYWKASGAEYDDOTSOREKEDDVFPGSGHTVWQVLEKNCPNAPSPLCLTYSYLSH 180

Qy	181	VDLVKDLNSGLIGALLVCRESGLAKERTQTLHKPILLFAVPDEGKSWHSETKNSIMODRR	240
Db	181	VDLVKDLNSGLIGALLVCRESGLAKERTQTLHKPILLFAVPDEGKSWHSETKNSIMODRR	240
Qy	241	AASARAMPKMHVYNGVYNSLPGLIGCHKRSVYWHVIGCTTPEVHSIFLEGHTFLVRNH	300
Db	241	AASARAMPKMHVYNGVYNSLPGLIGCHKRSVYWHVIGCTTPEVHSIFLEGHTFLVRNH	300
Qy	301	QASLEISPTFLTAOTLLMDLGOFLLECHSISHOHGMEAVYKVDSCPEEPQLRMKNNE	360
Db	301	QASLEISPTFLTAOTLLMDLGOFLLECHSISHOHGMEAVYKVDSCPEEPQLRMKNNE	360
Qy	361	EAEYDDDLDSBMDVYRFDNDNSPFIOTRSVAKKHPTWHTYTAABEEDMDAPLYLA	420
Db	361	EAEYDDDLDSBMDVYRFDNDNSPFIOTRSVAKKHPTWHTYTAABEEDMDAPLYLA	420
Qy	421	PDPRSYSQYLANNGPQIRGRTKKYKRPMAITDEFTKTRBAIOHESGILGPLLYGEVDYL	480
Db	421	PDPRSYSQYLANNGPQIRGRTKKYKRPMAITDEFTKTRBAIOHESGILGPLLYGEVDYL	480
Qy	481	LIFKNOASRPNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPEEIFKYKMTVTVEDGE	540
Db	481	LIFKNOASRPNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPEEIFKYKMTVTVEDGE	540
Qy	541	TKSDPCLTRVYSSFPVNMERDLASGLIGPILICVKSVDORNOIMSDKRWILLESVDE	600
Db	541	TKSDPCLTRVYSSFPVNMERDLASGLIGPILICVKSVDORNOIMSDKRWILLESVDE	600
Qy	601	NRSWLTENIORFLPNPAGVQLEDEFOASNMHSINGVYFDSLOSVCLHEVAYWYILS	660
Db	601	NRSWLTENIORFLPNPAGVQLEDEFOASNMHSINGVYFDSLOSVCLHEVAYWYILS	660
Qy	661	IGAOTDELSVFESGYFFKHKMAYEDTLTFPFSGEYFVMSMENPGIMLIGCHNSDFNRG	720
Db	661	IGAOTDELSVFESGYFFKHKMAYEDTLTFPFSGEYFVMSMENPGIMLIGCHNSDFNRG	720
Qy	721	MTALLKVSQCDKNTGYVEDSYEDISATILSKNNAIIPRSFSONRHSSTOKOPNATTT	780
Db	721	MTALLKVSQCDKNTGYVEDSYEDISATILSKNNAIIPRSFSONRHSSTOKOPNATTT	780
Qy	781	PBNDIEKTDPMFAHRTPMFKIONVSSDMLMLLRQSFPRGSLSDLOPAKYETFSDDPS	840
Db	781	PBNDIEKTDPMFAHRTPMFKIONVSSDMLMLLRQSFPRGSLSDLOPAKYETFSDDPS	840
Qy	841	PGAIDSNNSLSEMTHERPOLHHSQDMVTPPESGLQLELNKLGATTAATELKKLDFKYSST	900
Db	841	PGAIDSNNSLSEMTHERPOLHHSQDMVTPPESGLQLELNKLGATTAATELKKLDFKYSST	900
Qy	901	SNNLISPTPSDNLAACTDNTSSLAGPSMRYHDSQIDTTLFGKSSPLTEGGGSLSEE	960
Db	901	SNNLISPTPSDNLAACTDNTSSLAGPSMRYHDSQIDTTLFGKSSPLTEGGGSLSEE	960
Qy	961	NNDKSLLESGLMNSOESSWGKNVSTESGRLEFKKRAHGFPALLTXKNMLFYVYSISLLKTN	1020
Db	961	NNDKSLLESGLMNSOESSWGKNVSTESGRLEFKKRAHGFPALLTXKNMLFYVYSISLLKTN	1020
Qy	1021	KTSNNSATNRKTHIDPSSLIENSPSYQNTLESDTEFFKVPPLIHDRMLDKNATLRL	1080
Db	1021	KTSNNSATNRKTHIDPSSLIENSPSYQNTLESDTEFFKVPPLIHDRMLDKNATLRL	1080
Qy	1081	NHMSKTTSSKNMNMVQOKKEGPITPPDAQNDMSFFKMLFLPESAKWIORHGKNSLNSG	1140
Db	1081	NHMSKTTSSKNMNMVQOKKEGPITPPDAQNDMSFFKMLFLPESAKWIORHGKNSLNSG	1140
Qy	1141	QGPSPKQVLSLGPESVEGONFLSEKNVYVVGKEEFTKDVGLKEWFFSSRNLEFLJMLDN	1200
Db	1141	QGPSPKQVLSLGPESVEGONFLSEKNVYVVGKEEFTKDVGLKEWFFSSRNLEFLJMLDN	1200
Qy	1201	LHENTHNOEKKIOEBIEKKEKTLIOENVLPQIHTVIGIKNFKNLFLILSTRONVBSYD	1260
Db	1201	LHENTHNOEKKIOEBIEKKEKTLIOENVLPQIHTVIGIKNFKNLFLILSTRONVBSYD	1260

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Qy	1261	GATAPVLQDEFRSLNDSTNRKKTHTAHFSKKGEEBNEGLGNQTKOIVEKACTTRISPNT	1320
Db	1261	GATAPVLQDEFRSLNDSTNRKKTHTAHFSKKGEEBNEGLGNQTKOIVEKACTTRISPNT	1320
Qy	1321	SOQNFVQSRKRLKQFLPLEEFTLEKRIITVDSTQWSKMKKLLTSTLTQDINEKE	1380
Db	1321	SOQNFVQSRKRLKQFLPLEEFTLEKRIITVDSTQWSKMKKLLTSTLTQDINEKE	1380
Qy	1381	KGAIQOSPLDCLTRSHSIPQANRSPULIKVSSPFSIPILVTRVLEPQDNSSHLPAASY	1440
Db	1381	KGAIQOSPLDCLTRSHSIPQANRSPULIKVSSPFSIPILVTRVLEPQDNSSHLPAASY	1440
Qy	1441	RKDSGVQESSHFLQAKKNNLSLAILLEMTGQDREVSIGTSATNSGVYKKYENTVLP	1500
Db	1441	RKDSGVQESSHFLQAKKNNLSLAILLEMTGQDREVSIGTSATNSGVYKKYENTVLP	1500
Qy	1501	KPDLPKTSKVELLPVNYLYQKDLFPETTSNGSPGHLDVBSGLQGTREGAIKKNENNR	1560
Db	1501	KPDLPKTSKVELLPVNYLYQKDLFPETTSNGSPGHLDVBSGLQGTREGAIKKNENNR	1560
Qy	1561	GKVPFLVATESSAKTPSKLIDPLAMDNNHGTQIPKEEMKSOEKSPERTAKKKDTLLSL	1620
Db	1561	GKVPFLVATESSAKTPSKLIDPLAMDNNHGTQIPKEEMKSOEKSPERTAKKKDTLLSL	1620
Qy	1621	NACSNHAIATAINEGONKPEIVTMAKQGPTRERCSQNPVYLKRHOREITRTTQSDQEE	1680
Db	1621	NACSNHAIATAINEGONKPEIVTMAKQGPTRERCSQNPVYLKRHOREITRTTQSDQEE	1680
Qy	1681	IDYDDTISVEKKEDFDIYDEENOSPRSFOKTKRHYFLAABRLMDYGMSSSPHYLRNR	1740
Db	1681	IDYDDTISVEKKEDFDIYDEENOSPRSFOKTKRHYFLAABRLMDYGMSSSPHYLRNR	1740
Qy	1741	AQSGSVQPFKKVYFOEFTDGSFTQLYGELNEHLGLGPYIAAEVDNIWVTRNOASR	1800
Db	1741	AQSGSVQPFKKVYFOEFTDGSFTQLYGELNEHLGLGPYIAAEVDNIWVTRNOASR	1800
Qy	1801	PYSFYSLSIEEDQOGAEPKKNVYKNEFKYTKFMKVONHMAPTKDEPDCKAARYSDV	1860
Db	1801	PYSFYSLSIEEDQOGAEPKKNVYKNEFKYTKFMKVONHMAPTKDEPDCKAARYSDV	1860
Qy	1861	DLEKDVHSGILGPLLYCHNTNLPNAGNQVTFEALFTTIDETKSMYFENNERCRA	1920
Db	1861	DLEKDVHSGILGPLLYCHNTNLPNAGNQVTFEALFTTIDETKSMYFENNERCRA	1920
Qy	1921	PCNIOMEPTFEKENYFFHAINGYINDTLPGIYMAODRIKMYLLSWSNENHSHIFSGH	1980
Db	1921	PCNIOMEPTFEKENYFFHAINGYINDTLPGIYMAODRIKMYLLSWSNENHSHIFSGH	1980
Qy	1981	VFTYAKKKEEYKMAIYNYPGVEYVEMLPKAGIWRRECLIGBHLHAGSTLFLVYSNKC	2040
Db	1981	VFTYAKKKEEYKMAIYNYPGVEYVEMLPKAGIWRRECLIGBHLHAGSTLFLVYSNKC	2040
Qy	2041	QTPILGMAHGRDFOQTASGOYGONAPKLARLHYSGSINAMSTKEPFSWIKVLLAPMT	2100
Db	2041	QTPILGMAHGRDFOQTASGOYGONAPKLARLHYSGSINAMSTKEPFSWIKVLLAPMT	2100
Qy	2101	HGIKTQARQKQFSSLYISOFTIMYSLDKKKQYTRGNSGTTLWVFFGAVDSGKIHNFN	2160
Db	2101	HGIKTQARQKQFSSLYISOFTIMYSLDKKKQYTRGNSGTTLWVFFGAVDSGKIHNFN	2160
Qy	2161	PTIARTYRLHPHTYSTRJSTLAMELMGCDLNSCMPJGMSKRAISDAQITVASSTYTNMFA	2220
Db	2161	PTIARTYRLHPHTYSTRJSTLAMELMGCDLNSCMPJGMSKRAISDAQITVASSTYTNMFA	2220
Qy	2221	TWSPSKARLHLQGSNANRPQVNNKRWIYQDFQKTKVYGVGTQGVSSLLTSMYKVEFL	2280
Db	2221	TWSPSKARLHLQGSNANRPQVNNKRWIYQDFQKTKVYGVGTQGVSSLLTSMYKVEFL	2280
Qy	2281	ISSSDQHMTLFFQNGKRYVQGNQDSFTPVVNSLDPLRLRYLRIRIQOSWVQIOLRM	2340
Db	2281	ISSSDQHMTLFFQNGKRYVQGNQDSFTPVVNSLDPLRLRYLRIRIQOSWVQIOLRM	2340
Qy	2341	EVLGCEADOLY 2351	

Db 2341 EVLGEADLY 2351

## RESULT 29

AAW11404

ID AAW11404 standard; Protein; 2351 AA.

XX AAW11404;

XX 20-NOV-1997 (first entry)

XX Active Factor VIII:C analogue, delta 746, + residue 745 insertion.

XX Factor VIII:C analogue; glycoprotein; blood coagulation cascade;

KM fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;

KM plasma protease; thrombin; immunogen; antibody; haemophilia; therapy;

KM proteolytic cleavage.

XX

OS Homo sapiens.

XX Synthetic.

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Claim 24; Page -: 90pp; English.

AAW11330-W11472 represent active Factor VIII:C analogues of the invention. These sequences were created by mutating the wild type Factor VIII:C coding sequence (see AAT51357) using mutagenic primers. The analogues comprise a native Factor VIII:C polypeptide modified at a site adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg dipeptide is created. Factor VIII:C is a large glycoprotein that participates in the blood coagulation cascade that ultimately converts soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A deficiency in Factor VIII:C is responsible for haemophilia A, which is an X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is activated by plasma proteases, such as thrombin. During activation the mature polypeptide is cleaved to generate heavy and light chain fragments that are further cleaved. Complexes of two or more of the analogues, nucleic acids and vectors encoding them may be used alone or in

conjunction with each other, for the prevention or treatment of active Factor VIII:C deficiency in a mammal. The analogues may be used as immunogens to raise antibodies, and in the treatment of haemophilia, by improvement of haemostasis. The analogues are resistant to proteolytic cleavage and display increased plasma half-life. They may be administered at lower dosages and by different modes of administration.

XX Sequence 2351 AA:

Query Match 99.9%; Score 12408; DB 18; Length 2351;  
Best Local Similarity 99.9%; Pred. No. 0;  
Matches 2349; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

QY 1 MOELSTCFPLCLRCFSATRRYLGAELSDMDYQSDGLGELPDARFPFRPKSPFN 60  
DB 1 MOELSTCFPLCLRCFSATRRYLGAELSDMDYQSDGLGELPDARFPFRPKSPFN 60  
QY 61 TSYYKKTLVEFTDHLFNIAKPRPMGLGPTDAEYDVTVTLLKMAASHPSLHAY 120  
DB 61 TSYYKKTLVEFTDHLFNIAKPRPMGLGPTDAEYDVTVTLLKMAASHPSLHAY 120  
QY 121 GVSYWKASGAEAYDDQTSOREKEDKVPFGSHTYYWQVLKENGPMASDPLCLTYSLSH 180  
DB 121 GVSYWKASGAEAYDDQTSOREKEDKVPFGSHTYYWQVLKENGPMASDPLCLTYSLSH 180  
QY 181 VDLVKDLSGLIGALLVREGSLAKERTLHKEFILLFAVPEGKSMHSEFTKNSIMODRD 240  
DB 181 VDLVKDLSGLIGALLVREGSLAKERTLHKEFILLFAVPEGKSMHSEFTKNSIMODRD 240  
QY 241 AASARAMPKHTYNGVNSRLPGLIGCRKSYWNYIGCTTPEVHSTFLEGHTFLVRNH 300  
DB 241 AASARAMPKHTYNGVNSRLPGLIGCRKSYWNYIGCTTPEVHSTFLEGHTFLVRNH 300  
QY 241 AASARAMPKHTYNGVNSRLPGLIGCRKSYWNYIGCTTPEVHSTFLEGHTFLVRNH 300  
DB 241 AASARAMPKHTYNGVNSRLPGLIGCRKSYWNYIGCTTPEVHSTFLEGHTFLVRNH 300  
QY 301 ROASTDESPITFLTAOTLMDIGOLFCHISSHODGMEAYVYKSDSCPEPOLRMKNE 360  
DB 301 ROASTDESPITFLTAOTLMDIGOLFCHISSHODGMEAYVYKSDSCPEPOLRMKNE 360  
QY 361 EAEYDDDLTDSMDVYRFDONSPTQIORSVAKKHPTWVHYTAAEEDMYPAPLYLA 420  
DB 361 EAEYDDDLTDSMDVYRFDONSPTQIORSVAKKHPTWVHYTAAEEDMYPAPLYLA 420  
QY 421 PDDRSYKSOYLNNGPDRIGRKRYKRVMAATDFTFTRAIQIHESGILGVLGEVDTL 480  
DB 421 PDDRSYKSOYLNNGPDRIGRKRYKRVMAATDFTFTRAIQIHESGILGVLGEVDTL 480  
QY 481 LIIFKNQASRPYNIYPHGTTDVRPLYSRRLPKGVKHLKDFPLPGELFKYKWTYVEDGP 540  
DB 481 LIIFKNQASRPYNIYPHGTTDVRPLYSRRLPKGVKHLKDFPLPGELFKYKWTYVEDGP 540  
QY 541 TKSPDCLTYYSSPFVNMERDLASGLIGPLITCYKRSYORNOIMSDKRVLTFEVPDE 600  
DB 541 TKSPDCLTYYSSPFVNMERDLASGLIGPLITCYKRSYORNOIMSDKRVLTFEVPDE 600  
QY 601 NRSWYLTENIQFLPNPAGVQLEDPEFOASNMHSTNGVYFDSIQLSVCHAEVAYWYIIS 660  
DB 601 NRSWYLTENIQFLPNPAGVQLEDPEFOASNMHSTNGVYFDSIQLSVCHAEVAYWYIIS 660  
QY 661 IGAOTDPLSVFSGYTFKHKMYEDTLTLPFSGEYFVSMENPGIMTLGCHNSDFRNG 720  
DB 661 IGAOTDPLSVFSGYTFKHKMYEDTLTLPFSGEYFVSMENPGIMTLGCHNSDFRNG 720  
QY 721 MTALLKSSODKKTGQYEDSYEDISYVLSKNNALTEPSPQNSRRHPTROKOPNATTT 780  
DB 721 MTALLKSSODKKTGQYEDSYEDISYVLSKNNALTEPSPQNSRRHPTROKOPNATTT 780  
QY 781 PENDIEKTDWFAHRTPMKTONVSSDLMLLROSPTPHGISLSDQLEAKYEFSDDS 840  
DB 781 PENDIEKTDWFAHRTPMKTONVSSDLMLLROSPTPHGISLSDQLEAKYEFSDDS 840  
QY 841 PGALDSNNSISEMTHTRRQLHSGDMVTFEGSLQRLNEKIGTTAATLKKDKDFVYST 900  
DB 841 PGALDSNNSISEMTHTRRQLHSGDMVTFEGSLQRLNEKIGTTAATLKKDKDFVYST 900

Qy	901	SNNLSTIPSDNLAAGTDNTSSLGPPSMPVPHDLSQDLDTTLFGKSSPLTESGCPJLSEF	960
Db	901	SNNLSTIPSDNLAAGTDNTSSLGPPSMPVPHDLSQDLDTTLFGKSSPLTESGCPJLSEF	960
Qy	961	NNOSKLTBESGLMANSOESGMCKNVSPSEGRLEFKRRAGHALLTDMALFVYSISLKTN	1021
Db	961	NNOSKLTBESGLMANSOESGMCKNVSPSEGRLEFKRRAGHALLTDMALFVYSISLKTN	1021
Qy	1021	KTSNNSATNRKTHIDGSSLIENTSPWONILSDTEFFKKVYPLIHDMLDKNATALRL	1081
Db	1021	KTSNNSATNRKTHIDGSSLIENTSPWONILSDTEFFKKVYPLIHDMLDKNATALRL	1081
Qy	1081	NHMSNKTTSSKNMMEYOQKKEGIRPPDQNDPMSFFEMLELPEPSARWIOPTHGNNSLNSG	1141
Db	1081	NHMSNKTTSSKNMMEYOQKKEGIRPPDQNDPMSFFEMLELPEPSARWIOPTHGNNSLNSG	1141
Qy	1141	QGSPPKOLVSLGPRKSVYEQGNLSEKNKYVVGKEEFPKDGJLKEWFPSSBNLEFLTMDN	1201
Db	1141	QGSPPKOLVSLGPRKSVYEQGNLSEKNKYVVGKEEFPKDGJLKEWFPSSBNLEFLTMDN	1201
Qy	1201	LHENNTHNOEKKIOEELTEKKETLIOBNVLPQIHTVGTGNPKMLFLTLSTRONVESD	1261
Db	1201	LHENNTHNOEKKIOEELTEKKETLIOBNVLPQIHTVGTGNPKMLFLTLSTRONVESD	1261
Qy	1261	GAYAVLODFSLNDSTNRKTHAHSESKKEEBNLEGLANOTKIVKYACTTRISPT	1321
Db	1261	GAYAVLODFSLNDSTNRKTHAHSESKKEEBNLEGLANOTKIVKYACTTRISPT	1321
Qy	1321	SOONFVTOBSKRALQOFRLPEETLEFKRIIVDSTOWSKNMKHLPESTLOTDIYNEK	1381
Db	1321	SOONFVTOBSKRALQOFRLPEETLEFKRIIVDSTOWSKNMKHLPESTLOTDIYNEK	1381
Qy	1381	KGATQSPLOSCILTRHSITPOANBSPLIAVSSFPSSIRPYLTLYLEFODNSHLPAS	1441
Db	1381	KGATQSPLOSCILTRHSITPOANBSPLIAVSSFPSSIRPYLTLYLEFODNSHLPAS	1441
Qy	1441	RKSDGVOESHFLQAGAKNNLSALITLLEMTGQDREVSIGTSAITNSVTYKKYENTVPL	1501
Db	1441	RKSDGVOESHFLQAGAKNNLSALITLLEMTGQDREVSIGTSAITNSVTYKKYENTVPL	1501
Qy	1501	KFDLPKTSYGKELLPKYHLYOKDLPEPETSNGSPGHDLVESLLOCTEGEAKMNPANRP	1561
Db	1501	KFDLPKTSYGKELLPKYHLYOKDLPEPETSNGSPGHDLVESLLOCTEGEAKMNPANRP	1561
Qy	1561	GVPPPLRYATBESSAKTPSKLDPLAMDNIHGTOTIPEEKMISOEKSPEKTAFFKKOTILSL	1621
Db	1561	GVPPPLRYATBESSAKTPSKLDPLAMDNIHGTOTIPEEKMISOEKSPEKTAFFKKOTILSL	1621
Qy	1621	NACSENNHAIAINEGONKREIEVTAKQGRERLCSQNPVYLKRNORETRTLLOSDOE	1681
Db	1621	NACSENNHAIAINEGONKREIEVTAKQGRERLCSQNPVYLKRNORETRTLLOSDOE	1681
Qy	1681	IDYDDTISVEKKEDFDIYDEDENOSPRSFQKTRHFLTAVERLMDYGSSSPHYLNR	1741
Db	1681	IDYDDTISVEKKEDFDIYDEDENOSPRSFQKTRHFLTAVERLMDYGSSSPHYLNR	1741
Qy	1741	AQSGSVPOFKKVVFOEFTGSGFTOIRGELNHNGLLGRYRAREVDENITMVFRRQASR	1801
Db	1741	AQSGSVPOFKKVVFOEFTGSGFTOIRGELNHNGLLGRYRAREVDENITMVFRRQASR	1801
Qy	1801	PSTFSSSLISTEBEDQOAGERPKNFVAPNETKTYFVKVONHMAPTKDEPCKAMAFYS	1861
Db	1801	PSTFSSSLISTEBEDQOAGERPKNFVAPNETKTYFVKVONHMAPTKDEPCKAMAFYS	1861
Qy	1861	DLEKDVHSGILGVLACHNTLPNHNHGOYTVOERFLPFTJDEKFSMYTEMMENCSA	1921
Db	1861	DLEKDVHSGILGVLACHNTLPNHNHGOYTVOERFLPFTJDEKFSMYTEMMENCSA	1921
Qy	1921	PONTOMDEPFEKKNYFNAHNGYIMDTPLRGLVYAADORITRWLLSMGSSNENHSHFSGH	1981
Db	1921	PONTOMDEPFEKKNYFNAHNGYIMDTPLRGLVYAADORITRWLLSMGSSNENHSHFSGH	1981
Qy	1981	VFYAKKEEYKALVLYLPGVFEVEMJPKASIMNVEVELIGENHNAGMSTLEFLVYSKNC	2041

Db	1981	VFTYRKKEEYKMAIYLTVGVEYEMLEPSKAGIMVECLIGEHLAGSTLFLVYSNKC	2040
Qy	2041	QTPUGMASGHIIDFOITTAGSGOYGQWAPKLARLHYSGSINAMSTKEPFSWIKVDLLAPMI	2100
Db	2041	QTPUGMASGHIIDFOITTAGSGOYGQWAPKLARLHYSGSINAMSTKEPFSWIKVDLLAPMI	2100
Qy	2101	HGIKTQGARQKFSLLYSQFIIMYSLODKKMQTYRGNSITGLMVFPFGVNDSSGIRKHNI	2160
Db	2101	HGIKTQGARQKFSLLYSQFIIMYSLODKKMQTYRGNSITGLMVFPFGVNDSSGIRKHNI	2160
Qy	2161	PPRIARIIRLHPHYSINSTLMELMGCDLNSGMPUGMEBSKAISDAQITASSYFTNMA	2220
Db	2161	PPRIARIIRLHPHYSINSTLMELMGCDLNSGMPUGMEBSKAISDAQITASSYFTNMA	2220
Qy	2221	TWSPSKARLHLQGRSNAMPQVNNPKEMLQVDFQTKTKVTGVTQGVKSLTSMYVKEFL	2280
Db	2221	TWSPSKARLHLQGRSNAMPQVNNPKEMLQVDFQTKTKVTGVTQGVKSLTSMYVKEFL	2280
Qy	2281	ISSSQDGHQMTLFPQNGKVKYFQGNQDSFTPPVNSLDPELLTRYLRHPOSWVHQIALRM	2340
Db	2281	ISSSQDGHQMTLFPQNGKVKYFQGNQDSFTPPVNSLDPELLTRYLRHPOSWVHQIALRM	2340
Qy	2341	EVLGCEADPLY 2351	
Db	2341	EVLGCEADPLY 2351	
RESULT 30			
AA011456	AA011456 standard; Protein; 2352 AA.		
AA011456	20-NOV-1997 (first entry)		
DE	Active Factor VIII:C analogue residue 1719 P insertion.		
KW	Factor VIII:C; analogue; glycoprotein; blood coagulation cascade; fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis; plasma protease; thrombin; immunogen; antibody; haemophilic; therapy; proteolytic cleavage.		
OS	Homo sapiens.		
OS	Synthetic.		
PH	Key	Location/Qualifiers	
PH	Peptide	1..19	
FT		/note= "signal peptide"	
FT	Protein	20..2352	
FT		/note= "mature Factor VIII:C"	
FT	Region	20..1667	
FT		/note= "heavy chain fragment"	
FT	Region	1668..2351	
FT		/note= "light chain fragment"	
FT	Domain	760..1667	
FT		/note= "B domain"	
FT	Misc-difference	1738	
FT		/note= "inserted residue"	
PN	MO9703195-AI.		
PD	30-JAN-1997.		
PE	09-JUL-1996; 96WO-US11444.		
PR	11-JUL-1995; 95US-0001025.		
PA	(CHIR ) CHIRON CORP.		
PI	Cohen FE, Hung DT, Innis M;		
WP	1997-119050/11		

XX Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophilias, by improvement of  
PT haemostasis  
XX  
PS Claim 35; Page -: 90pp; English.  
XX  
XX AAM11330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophilias, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX  
SQ Sequence 2352 AA;  
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

QY 601 NRSWYLTENIQRFLEPNPAGVLEDPPEEQASNIHASTNGVPSDLSVCLHEAVYWTLS 660  
DB 601 NRSWYLTENIQRFLEPNPAGVLEDPPEEQASNIHASTNGVPSDLSVCLHEAVYWTLS 660  
QY 661 IGAQTFELSVFFSGYTFKHKMYEDDTLTLPFSGEIVFMSENPGLMTLGCNSDFRNRG 720  
DB 661 IGAQTFELSVFFSGYTFKHKMYEDDTLTLPFSGEIVFMSENPGLMTLGCNSDFRNRG 720  
QY 721 MTALLKVSQCKNTGDIYEDYEDISAVLLSKNNALERPESQNSRHSTQKOFNATTT 780  
DB 721 MTALLKVSQCKNTGDIYEDYEDISAVLLSKNNALERPESQNSRHSTQKOFNATTT 780  
QY 781 PENDIEKTPWFHARTPMKIQNVSSDLMMLROSPFHGLSLDLOEAKYETFSDDPS 840  
DB 781 PENDIEKTPWFHARTPMKIQNVSSDLMMLROSPFHGLSLDLOEAKYETFSDDPS 840  
QY 841 PGALDSNNSLSEMTHERPQLHHSQDMFTPESSGLRLNKEIGTAAATELKKLDFKYST 900  
DB 841 PGALDSNNSLSEMTHERPQLHHSQDMFTPESSGLRLNKEIGTAAATELKKLDFKYST 900  
QY 901 SNNLSTIPSDNLAAQDNTSSLGPPSPVHYDSQDLYTLFGKSSPITESGGPLSSEE 960  
DB 901 SNNLSTIPSDNLAAQDNTSSLGPPSPVHYDSQDLYTLFGKSSPITESGGPLSSEE 960  
QY 961 NNDKLLSEGLMSQSSSGKVVSTESGRIFGKRAHGAPALLTDMLPFVYSISLKTN 1020  
DB 961 NNDKLLSEGLMSQSSSGKVVSTESGRIFGKRAHGAPALLTDMLPFVYSISLKTN 1020  
QY 1021 KTSNNSATNKRTHIDGSPLLIENSPVONTLESDEFEKKVTPLIHDMKDNKNTALRL 1080  
DB 1021 KTSNNSATNKRTHIDGSPLLIENSPVONTLESDEFEKKVTPLIHDMKDNKNTALRL 1080  
QY 1081 NMSKNTTSSKNMEVQOKKEGPIPPDQNDPMSFEFMLFLEPSANWIOFRHGNKNSNG 1140  
DB 1081 NMSKNTTSSKNMEVQOKKEGPIPPDQNDPMSFEFMLFLEPSANWIOFRHGNKNSNG 1140  
QY 1141 QGSPKOLVSLGPEKVEGQNFSLSKNNVYVGKEFLKQVGLKEMVFPSSRLPLTINDN 1200  
DB 1141 QGSPKOLVSLGPEKVEGQNFSLSKNNVYVGKEFLKQVGLKEMVFPSSRLPLTINDN 1200  
QY 1201 LHENNTNOKKIQOEIELEKKEFLIOENVLPQITVTYGTAKFNKMLFLLSTRONVEGSYD 1260  
DB 1201 LHENNTNOKKIQOEIELEKKEFLIOENVLPQITVTYGTAKFNKMLFLLSTRONVEGSYD 1260  
QY 1261 GAYAPVLODFRSLNDSTNKTAKHTAHSEKKEEENLEGLNCTQKQVEXYACTPRISPNT 1320  
DB 1261 GAYAPVLODFRSLNDSTNKTAKHTAHSEKKEEENLEGLNCTQKQVEXYACTPRISPNT 1320  
QY 1321 SQONFVTQSRKRALQFRLPLEETELEKRIIIVDDTSTOWSKNNKHLTPSTLTQIDYNEKE 1380  
DB 1321 SQONFVTQSRKRALQFRLPLEETELEKRIIIVDDTSTOWSKNNKHLTPSTLTQIDYNEKE 1380  
QY 1381 KGATITOSPISDCLTRSHSTIPQANRSPRLTAIVSSPSTIRTYLTRVLFDQNSHLPASV 1440  
DB 1381 KGATITOSPISDCLTRSHSTIPQANRSPRLTAIVSSPSTIRTYLTRVLFDQNSHLPASV 1440  
QY 1441 RKKGSGVOESSHFLQGAKKNNLSLAILTLEMTGQREVGSLGTSATNSVYTKKVENTVLP 1500  
DB 1441 RKKGSGVOESSHFLQGAKKNNLSLAILTLEMTGQREVGSLGTSATNSVYTKKVENTVLP 1500  
QY 1501 KPDLPTKTSKVEYLLPVTYHIOYODLPPETSSNGSPGHLDIVGSLLOGTGALTKWNEANRP 1560  
DB 1501 KPDLPTKTSKVEYLLPVTYHIOYODLPPETSSNGSPGHLDIVGSLLOGTGALTKWNEANRP 1560  
QY 1561 GKVPFLVATESSAKTPSKLIDPLAMDHNHYGTQIPKEEMKSQSEKTAFFKKDPTILSL 1620  
DB 1561 GKVPFLVATESSAKTPSKLIDPLAMDHNHYGTQIPKEEMKSQSEKTAFFKKDPTILSL 1620  
QY 1621 NACESNNAIAAINEGQNKPEIETVAKQGRTERLCSQNPVYLKRHORREITRTTLOSDEE 1680  
DB 1621 NACESNNAIAAINEGQNKPEIETVAKQGRTERLCSQNPVYLKRHORREITRTTLOSDEE 1680

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QY 1681 IDYDDTISYEMKKEFDIYDEDENOSPRSFQKTRHFIYAVERLMDXGSSPHYL-RN 1739
    |||||||
Db 1681 IDYDDTISYEMKKEFDIYDEDENOSPRSQKTRHFIYAVERLMDXGSSPHYL-RN 1740
QY 1740 RAOSGSVPQKVVQOETDGSFTQPIYRGELNEHGLGPIYRAVEDNIMYTERNQS 1799
    |||||||
Db 1741 RAOSGSVPQKVVQOETDGSFTQPIYRGELNEHGLGPIYRAVEDNIMYTERNQS 1800
QY 1800 RPYSPYSSLIYEEDROGAPBRKNFYKPNETKYTFWKVOHMAPTKDEPCKAMAFSD 1859
    |||||||
Db 1801 RPYSPYSSLIYEEDROGAPBRKNFYKPNETKYTFWKVOHMAPTKDEPCKAMAFSD 1860
QY 1860 VDLEKDVHSLGLPIILYCHNTLNPARGROYTOEALFETTEDTSKMYTEMERNR 1919
    |||||||
Db 1861 VDLEKDVHSLGLPIILYCHNTLNPARGROYTOEALFETTEDTSKMYTEMERNR 1920
QY 1920 APCNIOMEDPTEKENYRPHAINGYIMDTLPGLVMAODQIRIHWYLLSMGSENHISIHFSG 1979
    |||||||
Db 1921 APCNIOMEDPTEKENYRPHAINGYIMDTLPGLVMAODQIRIHWYLLSMGSENHISIHFSG 1980
QY 1980 HFTVRKKEEYKALYNLYPGVFETVEMLPKAGIRVECLIGEHLHAGNSTLFLVYSNK 2039
    |||||||
Db 1981 HFTVRKKEEYKALYNLYPGVFETVEMLPKAGIRVECLIGEHLHAGNSTLFLVYSNK 2040
QY 2040 CQPIGMAQHTRDQIYASGOYGNAPKIALRHYSGSINAMSTKEPSTAKYDLAPM 2099
    |||||||
Db 2041 CQPIGMAQHTRDQIYASGOYGNAPKIALRHYSGSINAMSTKEPSTAKYDLAPM 2100
QY 2100 IHGIKTOGAROKFSSLYISQFIYMSLDGRKWOYRGNSTGTLMVFGVNDSSGIRKHNIF 2159
    |||||||
Db 2101 IHGIKTOGAROKFSSLYISQFIYMSLDGRKWOYRGNSTGTLMVFGVNDSSGIRKHNIF 2160
QY 2160 NPPIIARYIRLHPHTHSIRKSTLRMELGCDLNSCSPMLGMEKASIDQIYASSYFTNMF 2219
    |||||||
Db 2161 NPPIIARYIRLHPHTHSIRKSTLRMELGCDLNSCSPMLGMEKASIDQIYASSYFTNMF 2220
QY 2220 ATWSPSKARLHLOGSNMARPQVNNPKENIQVDFQKIMYVYTTQGYKSLTSMYKKEP 2279
    |||||||
Db 2221 ATWSPSKARLHLOGSNMARPQVNNPKENIQVDFQKIMYVYTTQGYKSLTSMYKKEP 2280
QY 2280 LISSSDGQHWTLFQNGKVKVFOGNDSTFPVANSIDPRLTTRYLRITHPQSVHWQIALR 2339
    |||||||
Db 2281 LISSSDGQHWTLFQNGKVKVFOGNDSTFPVANSIDPRLTTRYLRITHPQSVHWQIALR 2340
QY 2340 MEVLGCEADPLY 2351
    |||||||
Db 2341 MEVLGCEADPLY 2352

RESULT 31
AAW11458
ID AAW11458 standard; Protein; 2352 AA.
XX
AC AAW11458;
XX
DT 20-NOV-1997 (first entry)
XX
DE Active Factor VIII:C analogue residue 1720 P insertion.
XX
KM Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KM fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KM plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;
KM proteolytic cleavage.
XX
OS Homo sapiens.
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Peptide 1..19
FT Protein /note= "signal peptide"
FT /note= "mature Factor VIII:C"
FT Region 20..1667

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FT /note= "heavy chain fragment"
FT 1688..2351
FT /note= "light chain fragment"
FT Domain 760..1667
FT /note= "B domain"
FT Misc-difference 1739
FT /note= "inserted residue"
PN MO9703195-A1.
XX
PD 30-JAN-1997.
XX
PF 09-JUL-1996; 96MO-US11444.
XX
PR 11-JUL-1995; 95US-0001025.
XX
PA (CHIR ) CHIRON CORP.
PI Cohen FE, Hung DT, Innis M;
XX
DR WPI: 1997-119050/11.
XX
PT Factor VIII:C analog modified adjacent to a non-activating Arg
PT residue - used in the treatment of haemophilia, by improvement of
PT haemostasis
PS Claim 35; Page -: 90pp; English.
XX
XX AAW11330-M11472 represent active Factor VIII:C analogues of the
CC invention. These sequences were created by mutating the wild type Factor
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC analogues comprise a native Factor VIII:C polypeptide modified at a site
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC dipeptide is created. Factor VIII:C is a large glycoprotein that
CC participates in the blood coagulation cascade that ultimately converts
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC activated by plasma proteases, such as thrombin. During activation the
CC mature polypeptide is cleaved to generate heavy and light chain fragments
CC that are further cleaved. Complexes of two or more of the analogues,
CC nucleic acids and vectors encoding them may be used alone or in
CC conjunction with each other, for the prevention or treatment of active
CC Factor VIII:C deficiency in a mammal. The analogues may be used as
CC immunogens to raise antibodies, and in the treatment of haemophilia, by
CC improvement of haemostasis. The analogues are resistant to proteolytic
CC cleavage and display increased plasma half-life. They may be administered
CC at lower dosages and by different modes of administration.
XX
SQ Sequence 2352 AA.
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;
Best Local Similarity 100.0%; Pred. No. 0;
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;
QY 1 MOELSTCFPLCLARCFSATPRRYIAGVELSMDYMOSSLGFLPYDAFPPRPKSPFN 60
    |||||||
Db 1 MOELSTCFPLCLARCFSATPRRYIAGVELSMDYMOSSLGFLPYDAFPPRPKSPFN 60
QY 61 TSVYVKKTLEVEETHDLFNIAKPRPPMGLGPTQAEVYDRTVITLKNMASHVSLHAY 120
    |||||||
Db 61 TSVYVKKTLEVEETHDLFNIAKPRPPMGLGPTQAEVYDRTVITLKNMASHVSLHAY 120
QY 121 GVSYWKASGAEYDDQTSOREKEDKVPFGSGSHYVWQVLKENGPMASDPLCLTYSLSH 180
    |||||||
Db 121 GVSYWKASGAEYDDQTSOREKEDKVPFGSGSHYVWQVLKENGPMASDPLCLTYSLSH 180
QY 181 VDLVKDINSGLIGALLVCGESGLAKKKTQTLNHPITLFPVDEGKSMHSEPKNSLMQDDR 240
    |||||||
Db 181 VDLVKDINSGLIGALLVCGESGLAKKKTQTLNHPITLFPVDEGKSMHSEPKNSLMQDDR 240
QY 241 AASARAMPKMTVNGVYNSLPGILGCHRRSVYWHVIGGTTPEVHSLTEGHTFLVLRNH 300
    |||||||

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241 AASRAMPKMHVYGVNRSLEGLICHRKSVYWHVIGMCTTPEVHSTLELGHTEFLVRNH 300  
QY 301 ~~ROASHLEISPTTFLTAOFLTLMIDGOFLFCHISHOHGDEAVYKVDSCPEPOLRMKNE~~ 360  
Db 301 ~~ROASHLEISPTTFLTAOFLTLMIDGOFLFCHISHOHGDEAVYKVDSCPEPOLRMKNE~~ 360  
QY 361 EAEYDDDLTDSBMDVYRFDONSPSFQIQRSAKKHPRKTWHYIAADEMDVAPLYLA 420  
Db 361 EAEYDDDLTDSBMDVYRFDONSPSFQIQRSAKKHPRKTWHYIAADEMDVAPLYLA 420  
QY 421 PDDRSYKSOYLNGRPGRGKRYKKYRPMATDEFTKTRAIQIHESGILLGLYEGDUL 480  
Db 421 PDDRSYKSOYLNGRPGRGKRYKKYRPMATDEFTKTRAIQIHESGILLGLYEGDUL 480  
QY 481 LIFKQASRPYNYPHGTTIDVRPLYSRRLPKGVKHLKDFPILPQELIKYKWTYVEDG 540  
Db 481 LIFKQASRPYNYPHGTTIDVRPLYSRRLPKGVKHLKDFPILPQELIKYKWTYVEDG 540  
QY 541 TKSDPRLCTRYSSFPVNMERDLASGLIPLLICYKESVDORGNQIMSDKRVILFSYDE 600  
Db 541 TKSDPRLCTRYSSFPVNMERDLASGLIPLLICYKESVDORGNQIMSDKRVILFSYDE 600  
QY 601 NRSWYLTENIQRLPRPAGVQLEDPFQASINHASINGYVDSIQSLCYLAEVAYWTIIS 660  
Db 601 NRSWYLTENIQRLPRPAGVQLEDPFQASINHASINGYVDSIQSLCYLAEVAYWTIIS 660  
QY 661 IGAOTDFLSVFFSGYTFKHKWYEDTLTLPFSQETVFMSEMENPGLMTLGCNHSDFRNQ 720  
Db 661 IGAOTDFLSVFFSGYTFKHKWYEDTLTLPFSQETVFMSEMENPGLMTLGCNHSDFRNQ 720  
QY 721 MTALLKYSQCDKMTGYYEDSYEDISAYLISKNNALIEPRFSQNRHSTOKOFNATTI 780  
Db 721 MTALLKYSQCDKMTGYYEDSYEDISAYLISKNNALIEPRFSQNRHSTOKOFNATTI 780  
QY 781 PENDIEKTDWPAHRTPMFKIQNVSSDULMLRQSPTHGLSISDLOEAKYETFSDDBS 840  
Db 781 PENDIEKTDWPAHRTPMFKIQNVSSDULMLRQSPTHGLSISDLOEAKYETFSDDBS 840  
QY 841 PGALDSNNLSLEMTHERPOLHSGDMVTFESGLQRLNEKIGTTAAATELKIDFKVSSP 900  
Db 841 PGALDSNNLSLEMTHERPOLHSGDMVTFESGLQRLNEKIGTTAAATELKIDFKVSSP 900  
QY 901 SNNLISPTSDNLAACTDNTSLGPPSMAPHYASOJDTLTPKKSPLTESGGLSISE 960  
Db 901 SNNLISPTSDNLAACTDNTSLGPPSMAPHYASOJDTLTPKKSPLTESGGLSISE 960  
QY 961 NNSDKLLESGLMNSQESSGKAVSSTESGRLEFKGRAGPALLTKDNALFEVSIISLKTN 1020  
Db 961 NNSDKLLESGLMNSQESSGKAVSSTESGRLEFKGRAGPALLTKDNALFEVSIISLKTN 1020  
QY 1021 KTSNNSATNRKTHIDPSPILLENSPWNILSDTEFKKVTPLTHDMKMDKATATLRL 1080  
Db 1021 KTSNNSATNRKTHIDPSPILLENSPWNILSDTEFKKVTPLTHDMKMDKATATLRL 1080  
QY 1081 NHMSKNTSSKNMWEQOKKEGPIPPDAONPDMSPFKMALFLPESARWQORHGKNSLNSG 1140  
Db 1081 NHMSKNTSSKNMWEQOKKEGPIPPDAONPDMSPFKMALFLPESARWQORHGKNSLNSG 1140  
QY 1141 QGSPKOLVSLGPEKSVESQNTLSEKNKVVVGGEFTKDVGLKEVFPSSNLFITMLDN 1200  
Db 1141 QGSPKOLVSLGPEKSVESQNTLSEKNKVVVGGEFTKDVGLKEVFPSSNLFITMLDN 1200  
QY 1201 LHENNTHNOEKKLOEIEKKEKTLQOENNVLPOLHTYTGKNNMKRLFLSTRQWVGSQSD 1260  
Db 1201 LHENNTHNOEKKLOEIEKKEKTLQOENNVLPOLHTYTGKNNMKRLFLSTRQWVGSQSD 1260  
QY 1261 GAYAPVLQDFRSLNDSTNRTKHTAHFSKKGEEENLEGLGNQTOYEVKACTRISPM 1320  
Db 1261 GAYAPVLQDFRSLNDSTNRTKHTAHFSKKGEEENLEGLGNQTOYEVKACTRISPM 1320  
QY 1321 SQONFVTOFSKRALKQFLPLEETELEKRIITYDSTQOSKMMKHLFPLSTLJOIDYNEKE 1380  
Db 1321 SQONFVTOFSKRALKQFLPLEETELEKRIITYDSTQOSKMMKHLFPLSTLJOIDYNEKE 1380

QY 1361 KGAITQSPUSDCLTJNSHSTIQANRSPPLIAKVSFSPSTPIYLRLRVLEPDONSSHLPAS 1440  
Db 1361 KGAITQSPUSDCLTJNSHSTIQANRSPPLIAKVSFSPSTPIYLRLRVLEPDONSSHLPAS 1440  
QY 1441 RKKDSGVQESSHFLQAGAKNNLSLATITLPMGTQDQREVSGTSAFNSVYTKKVEWTVLP 1500  
Db 1441 RKKDSGVQESSHFLQAGAKNNLSLATITLPMGTQDQREVSGTSAFNSVYTKKVEWTVLP 1500  
QY 1501 KPDLPKTSKGVLELTKVHLYOKDLFPRETSGSPGHLQVBSLQSGEGATKWNANRP 1560  
Db 1501 KPDLPKTSKGVLELTKVHLYOKDLFPRETSGSPGHLQVBSLQSGEGATKWNANRP 1560  
QY 1561 GKVPFLRVATESAKTPSKLLDPLAMDNHGTQIPKEEKSQESKPEKTAFAKKDITLSL 1620  
Db 1561 GKVPFLRVATESAKTPSKLLDPLAMDNHGTQIPKEEKSQESKPEKTAFAKKDITLSL 1620  
QY 1621 NACSNNAIAIINEGQNKPELEVTMAQRTERLCSQNPVYLKRHOREIRTRTLOQDOE 1680  
Db 1621 NACSNNAIAIINEGQNKPELEVTMAQRTERLCSQNPVYLKRHOREIRTRTLOQDOE 1680  
QY 1681 IDYDDTISVENMKEDPDYIDDEMQSPRSQKTRHYFLAVERLMDYGMSSPHYLRN- 1739  
Db 1681 IDYDDTISVENMKEDPDYIDDEMQSPRSQKTRHYFLAVERLMDYGMSSPHYLRN- 1740  
QY 1740 RAQGSVPOFKKVVQOEFITDGSFTQPLYRGELNEHLGLGPYIRAEVDNIMVTFRNQAS 1799  
Db 1741 RAQGSVPOFKKVVQOEFITDGSFTQPLYRGELNEHLGLGPYIRAEVDNIMVTFRNQAS 1800  
QY 1800 RPYSFYSLSIYEEBOGQAGPRKNFVKPRNETYTKWQVQNHMAPTDDEDFCKAMVYFSD 1859  
Db 1801 RPYSFYSLSIYEEBOGQAGPRKNFVKPRNETYTKWQVQNHMAPTDDEDFCKAMVYFSD 1860  
QY 1860 VDLEKDVHSLGJLPVLYCHTNTLAPHAGROYVQEPALFFITIDETKSWTFENMRNCR 1919  
Db 1861 VDLEKDVHSLGJLPVLYCHTNTLAPHAGROYVQEPALFFITIDETKSWTFENMRNCR 1920  
QY 1920 APCNIQMEDPTFENYRPHAINGYIMDTLGLVMAODQIRIMVLLSGMSNENHSHIFSG 1979  
Db 1921 APCNIQMEDPTFENYRPHAINGYIMDTLGLVMAODQIRIMVLLSGMSNENHSHIFSG 1980  
QY 1980 HVTYVKKKEKYKALYNLYPGVFETVEMLPKSKGIMRVPCILGELHAGSTLFLVYSNK 2039  
Db 1981 HVTYVKKKEKYKALYNLYPGVFETVEMLPKSKGIMRVPCILGELHAGSTLFLVYSNK 2040  
QY 2040 CQPLGMAASHIRDOITASQOYQOMAPKLARLHSGSINAMSTKEPFSWKYDLAPMI 2099  
Db 2041 CQPLGMAASHIRDOITASQOYQOMAPKLARLHSGSINAMSTKEPFSWKYDLAPMI 2100  
QY 2100 IHGIKTQAGAKQKSSLYISOFLIMYSIDGKKQOTYRGNSTGTLMVFFGVNDSSGIKHNIF 2159  
Db 2101 IHGIKTQAGAKQKSSLYISOFLIMYSIDGKKQOTYRGNSTGTLMVFFGVNDSSGIKHNIF 2160  
QY 2160 NPPIIAYIRLHPHTHYSIRSLRRELGCGLNCSMPGLGMSKALISDAQTASSYTFNMF 2219  
Db 2161 NPPIIAYIRLHPHTHYSIRSLRRELGCGLNCSMPGLGMSKALISDAQTASSYTFNMF 2220  
QY 2220 ATWSPSKARLHLOGSNAWRQVANNPKEMLOVFOKTMKVTGVTTOGVKSLTSMYKVEF 2279  
Db 2221 ATWSPSKARLHLOGSNAWRQVANNPKEMLOVFOKTMKVTGVTTOGVKSLTSMYKVEF 2280  
QY 2280 LISSQODGQWTLFQONKVKVPGONDSTFPVANSLOPPLTIRLRIHQOSVWHQIALR 2339  
Db 2281 LISSQODGQWTLFQONKVKVPGONDSTFPVANSLOPPLTIRLRIHQOSVWHQIALR 2340  
QY 2340 MEVLGCEADOLY 2351  
Db 2341 MEVLGCEADOLY 2352

RESULT 32  
AAW11459 standard; protein; 2352 AA.  
ID AAW11459



[illegible]

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1021 KTSNNSATNKRTHIDGSLIENSPWONILSDTEFKKVPILLHDMLDKRAALRL 1080
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1081 NMSNKTSSKNMVEVOOKEGPIPPDAONPDMSFFKMLFLESARWIOPTHGKNSLNG 1140
1141 OGSPKOLVSLGPEKSVGONFLSEKKVYVGGEFTKDYGLKEVPPSSRNLFITNLN 1200
1141 OGSPKOLVSLGPEKSVGONFLSEKKVYVGGEFTKDYGLKEVPPSSRNLFITNLN 1200
1201 LHENNTHNOEKIOEEIEKKEITLQIENVVLPOIHTVGTGNPKMLFLSTRONVBSYD 1260
1261 GAYAPVLQDPRSLNDSJNTRKTHAFSKKEEENLEGLGNOTKOIVKRYACTRISPM 1320
1261 GAYAPVLQDPRSLNDSJNTRKTHAFSKKEEENLEGLGNOTKOIVKRYACTRISPM 1320
1321 SQONFTVQSKRAKQFRLPLEETLEKRLIVDSTONSKMKHLPTSTLQIDNEKE 1380
1321 SQONFTVQSKRAKQFRLPLEETLEKRLIVDSTONSKMKHLPTSTLQIDNEKE 1380
1381 KGATIOSPLSDCLTRSHSIPQANSPLPIAKVSSPSIRPIYLTVLFQDNSSHLPAAY 1440
1441 RKDSGVQESSHFLQAKKNNLSLAILLEMTGDQREVSIGTSTNTSVYKKVKNTP 1500
1441 RKDSGVQESSHFLQAKKNNLSLAILLEMTGDQREVSIGTSTNTSVYKKVKNTP 1500
1501 KPDLPTSGKVELLPVNIYQKDLPTETNSGSPGLDIVESGLQTEGAIKNEANRP 1560
1501 KPDLPTSGKVELLPVNIYQKDLPTETNSGSPGLDIVESGLQTEGAIKNEANRP 1560
1561 GKVPFLKVAATESAKTPSKLDPLAMDNHYGTQIPKEEKSOEKSPEKTAFFKKDTLST 1620
1561 GKVPFLKVAATESAKTPSKLDPLAMDNHYGTQIPKEEKSOEKSPEKTAFFKKDTLST 1620
1621 NACSNHAIINAGONKPEIEVMAKOGREPLCSGNPVYKRRORITPTTLOSQOE 1680
1621 NACSNHAIINAGONKPEIEVMAKOGREPLCSGNPVYKRRORITPTTLOSQOE 1680
1681 IDYDDTISVEMKKEPDIYDEENQSPSPQKTRHYFIAAVERLMDYGMSSPHYXLRN 1740
1681 IDYDDTISVEMKKEPDIYDEENQSPSPQKTRHYFIAAVERLMDYGMSSPHYXLRN 1740
1740 RAOSGSVPQFKKVFQEFSTQPLYRGELNEHGLGPYIRAEVDNIMVTFRQAS 1799
1740 RAOSGSVPQFKKVFQEFSTQPLYRGELNEHGLGPYIRAEVDNIMVTFRQAS 1799
1800 RPYFSYSLISYEEDROGAPRKPNFTYFMKVOHMAPTKDEPCKRAMAYESD 1859
1800 RPYFSYSLISYEEDROGAPRKPNFTYFMKVOHMAPTKDEPCKRAMAYESD 1859
1860 VDLEKDVHSLGIPLLVCHTNTLMPAHGROYVOEFALFTIETDKSWYFTEMERNCR 1919
1860 VDLEKDVHSLGIPLLVCHTNTLMPAHGROYVOEFALFTIETDKSWYFTEMERNCR 1919
1861 VDLEKDVHSLGIPLLVCHTNTLMPAHGROYVOEFALFTIETDKSWYFTEMERNCR 1920
1920 APCNIQMEDPTEKENYREHAIINGYIMDTLPGLVMAODQIRIYLLSMGSNNHISHFSG 1979
1920 APCNIQMEDPTEKENYREHAIINGYIMDTLPGLVMAODQIRIYLLSMGSNNHISHFSG 1979
1921 APCNIQMEDPTEKENYREHAIINGYIMDTLPGLVMAODQIRIYLLSMGSNNHISHFSG 1980
1980 HFTVVRKKEKXKALYLVGVFETVEMLSKAGIRVCLLGEHLHAGMSTFLVYSNK 2039
1980 HFTVVRKKEKXKALYLVGVFETVEMLSKAGIRVCLLGEHLHAGMSTFLVYSNK 2040
2040 CQPLGMAAGHINDFOITASGOYGOMAPKLARLHYSGSINAMSTKEPSSWIKVDLAPMI 2099
2040 CQPLGMAAGHINDFOITASGOYGOMAPKLARLHYSGSINAMSTKEPSSWIKVDLAPMI 2100
2100 IHGIRTOGAROKFSSLYISOFIWSIDGKKMOTYRGNSTGTLAMFRGNVDSGIRHNIF 2159

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2101 IHGIRTOGAROKFSSLYISOFIWSIDGKKMOTYRGNSTGTLAMFRGNVDSGIRHNIF 2160
2160 NPPIARVIRLHPTHYSTRSLRMELMGCDLNSCSMPJGMSKAIISAOITYASSYTNNE 2219
2161 NPPIARVIRLHPTHYSTRSLRMELMGCDLNSCSMPJGMSKAIISAOITYASSYTNNE 2220
2220 ATWSPSKARLHOGSRNMRPOVNNPKEMLOVDFOKTKMYTGTTOGVKSLLTSMYKEE 2279
2221 ATWSPSKARLHOGSRNMRPOVNNPKEMLOVDFOKTKMYTGTTOGVKSLLTSMYKEE 2280
2280 LISSQDGHQWTLFPONGKRVYFOGNDSTFPVNSLDPPLITRYLAIHQSVWHDIALR 2339
2281 LISSQDGHQWTLFPONGKRVYFOGNDSTFPVNSLDPPLITRYLAIHQSVWHDIALR 2340
2340 MEVLGCEADOLY 2351
2341 MEVLGCEADOLY 2352

RESULT 33
AAW11463
ID AAW11463 standard; Protein: 2352 AA.
XX
AC AAW11463;
XX
DT 21-NOV-1997 (first entry)
XX
DE Active Factor VIII:C analogue residue 1721 P insertion.
XX
KW Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;
KW proteolytic cleavage.
XX
OS Homo sapiens.
OS
XX
FH Key
FT 1..19 Location/Qualifiers
FT 20..2352 /note="signal peptide"
FT Protein /note="mature Factor VIII:C"
FT Region /note="heavy chain fragment"
FT Region /note="1667-2351"
FT Region /note="1191-1667"
FT Domain /note="B domain"
FT Misc-difference 1740 /note="inserted residue"
XX
PN WO9703195-A1.
XX
PD 30-JAN-1997.
XX
PF 09-JUL-1996; 96WO-US11444.
XX
PR 11-JUL-1995; 95US-0001025.
XX
PA (CHIR ) CHIRON CORP.
XX
PI Cohen FE, Hung DT, Innis M;
XX
DR WPI; 1997-119050/11.
XX
PT Factor VIII:C analog modified adjacent to a non-activating Arg
PT residue - used in the treatment of haemophilias, by improvement of
XX haemostasis
XX
PS Claim 37; Page -: 90pp; English.
XX
CC AAW11330-W11472 represent active Factor VIII:C analogues of the
CC invention. These sequences were created by mutating the wild type Factor

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CC	VIII:C coding sequence (see AAT51357) using mutagenic primers. The	OY	721	MTALLKVVSSCKNDGYEDSYEDISATYLLSKNNAIEPRFSQNSRHPSTROKQFNATTI	780
CC	analogues comprise a native Factor VIII:C polypeptide modified at a site	OY	721	MTALLKVVSSCKNDGYEDSYEDISATYLLSKNNAIEPRFSQNSRHPSTROKQFNATTI	780
CC	adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg	DB	721	MTALLKVVSSCKNDGYEDSYEDISATYLLSKNNAIEPRFSQNSRHPSTROKQFNATTI	780
CC	dipeptide is created. Factor VIII:C is a large glycoprotein that	OY	781	PENDIKETPMWNRHTPMKPIQNVSSSDLMILRQSPPHGLSLSDQEAKEVTSDDPS	840
CC	participates in the blood coagulation cascade that ultimately converts	DB	781	PENDIKETPMWNRHTPMKPIQNVSSSDLMILRQSPPHGLSLSDQEAKEVTSDDPS	840
CC	soluble fibrinogen to insoluble fibrin clot, effecting hemostasis. A	OY	841	PGALIDSNLSMTHFRQOLHNSDWMFTPEGLOLRLENKLTGTATATELKLDPKYST	900
CC	deficiency in Factor VIII:C is responsible for haemophilia A, which is an	DB	841	PGALIDSNLSMTHFRQOLHNSDWMFTPEGLOLRLENKLTGTATATELKLDPKYST	900
CC	x-chromosome-linked inherited bleeding diathesis. Factor VIII:C is	OY	961	NDSKLEEGGLNNSQESSMGKNVSSSTSGRLFKGRARGPALLTKDUALFKVISILKTN	1020
CC	activated by plasma proteases, such as thrombin. During activation the	DB	961	NDSKLEEGGLNNSQESSMGKNVSSSTSGRLFKGRARGPALLTKDUALFKVISILKTN	1020
CC	mature polypeptide is cleaved to generate heavy and light chain fragments	OY	1021	KTSNNSATNRKTHIDGSLILENPSVQNTLLESTPEKKYTPILIDRMIMKNTATRL	1080
CC	that are further cleaved. Complexes of two or more of the analogues,	DB	1021	KTSNNSATNRKTHIDGSLILENPSVQNTLLESTPEKKYTPILIDRMIMKNTATRL	1080
CC	nucleic acids and vectors encoding them may be used alone or in	OY	901	SNMLISTIPSDMLAAGTDNTSSLGAPSPMPVHYSDLDITTLFGKKSSPTRESGPLSIEE	960
CC	conjunction with each other, for the prevention or treatment of active	DB	901	SNMLISTIPSDMLAAGTDNTSSLGAPSPMPVHYSDLDITTLFGKKSSPTRESGPLSIEE	960
CC	Factor VIII:C deficiency in a mammal. The analogues may be used as	OY	1081	NHMSNKTSSKMMENVQOKKGPILPDAQNPMSFFKMLPLRESARVIQRTHGKNSLNSG	1140
CC	immunogens to raise antibodies, and in the treatment of haemophilias, by	DB	1081	NHMSNKTSSKMMENVQOKKGPILPDAQNPMSFFKMLPLRESARVIQRTHGKNSLNSG	1140
CC	improvement of haemostasis. The analogues are resistant to proteolytic	OY	1141	OGPSPKOLVSLGPEKSYGVGNFLSEKRVVYKGGFTDVCLKMVPSSRNPLFTLNID	1200
CC	cleavage and display increased plasma half-life. They may be administered	DB	1141	OGPSPKOLVSLGPEKSYGVGNFLSEKRVVYKGGFTDVCLKMVPSSRNPLFTLNID	1200
CC	at lower dosages and by different modes of administration.	OY	1201	LHENNTHNOEKKIOEIEFKKFTLQOENVVLPOLHTVYCTKPMKNLFLISTQONVSSYD	1260
CC		DB	1201	LHENNTHNOEKKIOEIEFKKFTLQOENVVLPOLHTVYCTKPMKNLFLISTQONVSSYD	1260
OY		OY	1261	GAYAPVLDQFRLSDNSTNRKTHAHFSPKGBEENLBSLGNOTKOIYEKACTTRISPT	1320
DB		DB	1261	GAYAPVLDQFRLSDNSTNRKTHAHFSPKGBEENLBSLGNOTKOIYEKACTTRISPT	1320
OY		OY	1321	SOONFYTQSKRALKQFRLPLEETLELEKRIYVDQTSQMSKNMHLPTSLYOIDYNEKE	1380
DB		DB	1321	SOONFYTQSKRALKQFRLPLEETLELEKRIYVDQTSQMSKNMHLPTSLYOIDYNEKE	1380
OY		OY	1381	KGATQSPISDCLTFRSHSIPQANSPSLPAKXSSPSPRIYTLRLVFDONSSHLPAAST	1440
DB		DB	1381	KGATQSPISDCLTFRSHSIPQANSPSLPAKXSSPSPRIYTLRLVFDONSSHLPAAST	1440
OY		OY	1441	RKDSGVQSSSHFLOGAKKNLALATLTLEMTGDQREVGSIGTSATNSVYKKVENTVLP	1500
DB		DB	1441	RKDSGVQSSSHFLOGAKKNLALATLTLEMTGDQREVGSIGTSATNSVYKKVENTVLP	1500
OY		OY	1501	KPDLPTSGKVELLPKVAHYOKDLFPEPTNSPGHLDVLGSLIGSTEGALIKMNEARP	1560
DB		DB	1501	KPDLPTSGKVELLPKVAHYOKDLFPEPTNSPGHLDVLGSLIGSTEGALIKMNEARP	1560
OY		OY	1561	GKVPFLVATSSSACTPCKLIDPLAMDNIHGTQIPREBKXQEKSPKTAFFKKDTIILSL	1620
DB		DB	1561	GKVPFLVATSSSACTPCKLIDPLAMDNIHGTQIPREBKXQEKSPKTAFFKKDTIILSL	1620
OY		OY	1621	NACESNHAIIAINEGONPBEIENVAKOGFTEKLSQNPVLAKRHQDEITRTTLODQEE	1680
DB		DB	1621	NACESNHAIIAINEGONPBEIENVAKOGFTEKLSQNPVLAKRHQDEITRTTLODQEE	1680
OY		OY	1681	IDYDDTISYEMKKEPFDYIDDEDNQSRSPQKKTTHRYFLAIVEKLMQYMGSSSPHYLKN	1739
DB		DB	1681	IDYDDTISYEMKKEPFDYIDDEDNQSRSPQKKTTHRYFLAIVEKLMQYMGSSSPHYLKN	1739
OY		OY	1740	RAQSGSYPOGKVVYVQFETDQSFQPLRYKGLLENHGLGPGYIAAEVDNIYNTFRNQS	1799
DB		DB	1741	RAQSGSYPOGKVVYVQFETDQSFQPLRYKGLLENHGLGPGYIAAEVDNIYNTFRNQS	1799
OY		OY	1800	RYVSFYSSLSIIEEDQROGAPRRNFKPDETKYFNVYQHHNAPPTDEDFDKAAVAYSD	1859
DB		DB	1800	RYVSFYSSLSIIEEDQROGAPRRNFKPDETKYFNVYQHHNAPPTDEDFDKAAVAYSD	1859

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Db      1801 RPYSFYSSLSIYEDDROGAEPRKRFVPRNETKTYEAKVOHNHAPLTKDEFCKAMAYFSD 1860
      |||
Qy      1860 VDLEKDVHSGILGPLLVCHTNTLNPAHGRVYVQVEAFLEFTJEDSKMYTEKMNENCR 1919
      |||
Db      1861 VDLEKDVHSGILGPLLVCHTNTLNPAHGRVYVQVEAFLEFTJEDSKMYTEKMNENCR 1920
      |||
Qy      1920 APCNIOMEDPTREKRNRFHAINGYIMDTLRLVLAADODRIRYLLSKGSNNHSHIFSG 1979
      |||
Db      1921 APCNIOMEDPTREKRNRFHAINGYIMDTLRLVLAADODRIRYLLSKGSNNHSHIFSG 1980
      |||
Qy      1980 HFTVRRKREYKMAIYNLYPGVFETVEMLPSKAGIWRVDECLIGEHLAGMSTLFLVYSNK 2039
      |||
Db      1981 HFTVRRKREYKMAIYNLYPGVFETVEMLPSKAGIWRVDECLIGEHLAGMSTLFLVYSNK 2040
      |||
Qy      2040 COTPLGMASGHINDPQITASGOYGOMAPKLARLHYSGSINASTKEPFSWIKVDLLAPMI 2099
      |||
Db      2041 COTPLGMASGHINDPQITASGOYGOMAPKLARLHYSGSINASTKEPFSWIKVDLLAPMI 2100
      |||
Qy      2100 IHGKTGAGAKRSSLYISQFTIMSLDGKRWQTYRGNSTGLMVFEGNVDSGIRKNIF 2159
      |||
Db      2101 IHGKTGAGAKRSSLYISQFTIMSLDGKRWQTYRGNSTGLMVFEGNVDSGIRKNIF 2160
      |||
Qy      2160 NPPIIARIHLPTHSIRSLRMLMCCDLNSCNPGLMESKASDAQITASSYFTNMF 2219
      |||
Db      2161 NPPIIARIHLPTHSIRSLRMLMCCDLNSCNPGLMESKASDAQITASSYFTNMF 2220
      |||
Qy      2220 ATWSPSKARLHLOGRSNAMPVNNPKEMLOVDFOKTMKVTVTGYGKSLTSMYKFE 2279
      |||
Db      2221 ATWSPSKARLHLOGRSNAMPVNNPKEMLOVDFOKTMKVTVTGYGKSLTSMYKFE 2280
      |||
Qy      2280 LISSQDGHQWTLFPGNGKVKYVFGQNDSTFPVYNSLDPPLTRLRIRHPDSWHQJALR 2339
      |||
Db      2281 LISSQDGHQWTLFPGNGKVKYVFGQNDSTFPVYNSLDPPLTRLRIRHPDSWHQJALR 2340
      |||
Qy      2340 MEVLGCEADPLY 2351
      |||
Db      2341 MEVLGCEADPLY 2352
      |||

RESULT 34
AAW11464
ID      AAW11464 standard; Protein; 2352 AA.
XX
AC      AAW11464;
XX
DT      21-NOV-1997 (first entry)
XX
DE      Active Factor VIII:C analogue residue 1722 P insertion.
XX
KW      Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KM      fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KM      plasma protease; thrombin; immunogen; antibody; haemophilias; therapy;
XX      proteolytic cleavage.
XX
OS      Homo sapiens.
OS      Synthetic.
XX
FH      Key
FT      Location/Qualifiers
FT      1..19
FT      /note= "signal peptide"
FT      Protein
FT      20..2352
FT      /note= "mature Factor VIII:C"
FT      Region
FT      20..1667
FT      /note= "heavy chain fragment"
FT      Region
FT      1668..2351
FT      /note= "light chain fragment"
FT      Domain
FT      760..1667
FT      /note= "B domain"
FT      Misc-difference 1741
FT      /note= "inserted residue"
XX
PN      WO9703195-A1.
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XX      30-JAN-1997.
PD
XX
XX      09-JUL-1996; 96NC-US11444.
PF
XX
PR      11-JUL-1995; 95US-0001025.
XX
XX      (CHIR ) CHIRON CORP.
XX
XX      Cohen FE, Hung DT, Innis M;
PI
XX      MPI; 1997-119050/11.
DR
XX
XX      Factor VIII:C analog modified adjacent to a non-activating Arg
PT      residue - used in the treatment of haemophilias, by improvement of
PT      haemostasis
PS
XX      Claim 37; Page -: 90pp; English.
XX
XX      AAW11330-W11472 represent active Factor VIII:C analogues of the
CC      invention. These sequences were created by mutating the wild type Factor
CC      VIII:C coding sequence (see AA51357) using mutagenic primers. The
CC      analogues comprise a native Factor VIII:C polypeptide modified at a site
CC      adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC      dipeptide is created. Factor VIII:C is a large glycoprotein that
CC      participates in the blood coagulation cascade that ultimately converts
CC      soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC      deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC      X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC      activated by plasma proteases, such as thrombin. During activation the
CC      mature polypeptide is cleaved to generate heavy and light chain fragments
CC      that are further cleaved. Complexes of two or more of the analogues,
CC      nucleic acids and vectors encoding them may be used alone or in
CC      conjunction with each other, for the prevention or treatment of active
CC      Factor VIII:C deficiency in a mammal. The analogues may be used as
CC      immunogens to raise antibodies, and in the treatment of haemophilias, by
CC      improvement of haemostasis. The analogues are resistant to proteolytic
CC      cleavage and display increased plasma half-life. They may be administered
CC      at lower dosages and by different modes of administration.
XX
SQ      Sequence 2352 AA:
XX
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;
Best Local Similarity 100.0%; Pred. No. 0;
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;
Qy      1 MOELSTCEFLCLLRFCFSATRRYYLGAVELSWDYQSDGLGELPYDARPPRYKSPFN 60
      |||
Db      1 MOELSTCEFLCLLRFCFSATRRYYLGAVELSWDYQSDGLGELPYDARPPRYKSPFN 60
      |||
Qy      61 TSVYKKTTLFVEPTDHLFNIAKPPPMGLGPTIOAEYVDVYITLKNNASHPVSLAHV 120
      |||
Db      61 TSVYKKTTLFVEPTDHLFNIAKPPPMGLGPTIOAEYVDVYITLKNNASHPVSLAHV 120
      |||
Qy      121 GVSYWKASBGALEYDQTSQREKEDDKYFGGSHYTYWYLYKBNPMA5DPLCTYYSLSH 180
      |||
Db      121 GVSYWKASBGALEYDQTSQREKEDDKYFGGSHYTYWYLYKBNPMA5DPLCTYYSLSH 180
      |||
Qy      121 GVSYWKASBGALEYDQTSQREKEDDKYFGGSHYTYWYLYKBNPMA5DPLCTYYSLSH 180
      |||
Db      121 GVSYWKASBGALEYDQTSQREKEDDKYFGGSHYTYWYLYKBNPMA5DPLCTYYSLSH 180
      |||
Qy      181 VDIYKDNLSGLIGALLVYREGSLAKKETOYLAKFTLLFAVDEDEKSNHSETKNSLQDDRD 240
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Db      181 VDIYKDNLSGLIGALLVYREGSLAKKETOYLAKFTLLFAVDEDEKSNHSETKNSLQDDRD 240
      |||
Qy      241 AASARAPKMHVNVNYSVNRSLPGLIGHRKSVYWHYIGGTPPEVHSTFEGTFLVRNH 300
      |||
Db      241 AASARAPKMHVNVNYSVNRSLPGLIGHRKSVYWHYIGGTPPEVHSTFEGTFLVRNH 300
      |||
Qy      301 RQASLEISPTITTAQDILLMDLGGFLLFCHISSHODGMEAYVVDSCPEEPOLRRKKNNE 360
      |||
Db      301 RQASLEISPTITTAQDILLMDLGGFLLFCHISSHODGMEAYVVDSCPEEPOLRRKKNNE 360
      |||
Qy      361 EAEYDDDLTDESEMDVYRFDDNSPSFIQIRSVAKKHPTVWHYIAAEEDMDVYAPLVLA 420
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Db      361 EAEYDDDLTDESEMDVYRFDDNSPSFIQIRSVAKKHPTVWHYIAAEEDMDVYAPLVLA 420
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Qy	421	PDDPSYTSQYLNNGPORGKRYKKVPRMAVTDTEFKTRPAIOHESGILGPLYGEVDTL	480
Dp	421	PDHDSYTSQYLNNGPORGKRYKKVPRMAVTDTEFKTRPAIOHESGILGPLYGEVDTL	480
Qy	481	LIFKNOASPRYAIYPHGITTDRPLYSRRILPKVCVKILKOPFLIEGGEJFKKMYVEDP	540
Dp	481	LIFKNOASPRYAIYPHGITTDRPLYSRRILPKVCVKILKOPFLIEGGEJFKKMYVEDP	540
Qy	541	TKSPROCLTRYESSPFNMEROLASGLILGPLLITCYKSYNOGRNOIMDKKNVILSFVPE	600
Dp	541	TKSPROCLTRYESSPFNMEROLASGLILGPLLITCYKSYNOGRNOIMDKKNVILSFVPE	600
Qy	601	NRSWYLTENTQRLPRPAGVOLDPEFOQASINMHSINGYEDSIQLSYCHAYAYIIS	660
Dp	601	NRSWYLTENTQRLPRPAGVOLDPEFOQASINMHSINGYEDSIQLSYCHAYAYIIS	660
Qy	661	IGAOTDELVSFESGYTFEKHKMYEDTLTLPPFSGETVFSMNEBGLITLCHNSDFRNG	720
Dp	661	IGAOTDELVSFESGYTFEKHKMYEDTLTLPPFSGETVFSMNEBGLITLCHNSDFRNG	720
Qy	721	MTALIKYSDCKMTQGYEDSYEDISAYLKSNNALTEPFSQNSRRPSTRQKOFANATY	780
Dp	721	MTALIKYSDCKMTQGYEDSYEDISAYLKSNNALTEPFSQNSRRPSTRQKOFANATY	780
Qy	781	PENIDEXTDWPFAHRPMFKIONYSSDILMLROSPPHGISLSDIOEAKYTFESDDPS	840
Dp	781	PENIDEXTDWPFAHRPMFKIONYSSDILMLROSPPHGISLSDIOEAKYTFESDDPS	840
Qy	841	PGAIDSNNSLSEMTWHRPQLHHSGDWVPFESGLOLRLEKGTAAATELKLDPFVYST	900
Dp	841	PGAIDSNNSLSEMTWHRPQLHHSGDWVPFESGLOLRLEKGTAAATELKLDPFVYST	900
Qy	901	SNNILISTIPBDNLAAOTDWTSLGPPSPMAYHYSQDITLTFEKKSSPLTESGGPLSLSE	960
Dp	901	SNNILISTIPBDNLAAOTDWTSLGPPSPMAYHYSQDITLTFEKKSSPLTESGGPLSLSE	960
Qy	961	NNDSKLLSEGLMNSOSSSGKMYSTSGSLPFGKRAHAPALLTKRDNALRKVYSISLTKN	1020
Dp	961	NNDSKLLSEGLMNSOSSSGKMYSTSGSLPFGKRAHAPALLTKRDNALRKVYSISLTKN	1020
Qy	1021	KTSNNSATNKRTHIDGPSLLIENSPWQNILSDTEFKRYVPLIHORMLMDNATALRL	1080
Dp	1021	KTSNNSATNKRTHIDGPSLLIENSPWQNILSDTEFKRYVPLIHORMLMDNATALRL	1080
Qy	1081	NHMSKRTTSSKNEMAYOQKKEGPITPPAONPDMSPFKMLTFEPESARWIOPTHKNSLNG	1140
Dp	1081	NHMSKRTTSSKNEMAYOQKKEGPITPPAONPDMSPFKMLTFEPESARWIOPTHKNSLNG	1140
Qy	1141	OGPSRKOLVSLGEXKEVEGONFLSKKNVYVGGEPTXOYGLKEVPPSSPNLFTNLND	1200
Dp	1141	OGPSRKOLVSLGEXKEVEGONFLSKKNVYVGGEPTXOYGLKEVPPSSPNLFTNLND	1200
Qy	1201	LHENNTNHOEKKLOEIEIEKKEFLIOENVVLPOLIHVYTGKKNFKMLFLILSTRONVEGSD	1260
Dp	1201	LHENNTNHOEKKLOEIEIEKKEFLIOENVVLPOLIHVYTGKKNFKMLFLILSTRONVEGSD	1260
Qy	1261	GAYAPVLQDERSLNDSTNTKTKHTAHSKSKGEEENLEGJNOKTOYEKYACTTJRISPMT	1320
Dp	1261	GAYAPVLQDERSLNDSTNTKTKHTAHSKSKGEEENLEGJNOKTOYEKYACTTJRISPMT	1320
Qy	1321	SOONPVYTORAKLAKOFRPLPEETLEKRIYVDJSTOKSKMKMLPSTLTQIDVNEKE	1380
Dp	1321	SOONPVYTORAKLAKOFRPLPEETLEKRIYVDJSTOKSKMKMLPSTLTQIDVNEKE	1380
Qy	1381	KGATQSPSLDCITRSHSITPOANSPLPIAKVSSPFSIRPYILRYVLFQDNSSHLPASAY	1440
Dp	1381	KGATQSPSLDCITRSHSITPOANSPLPIAKVSSPFSIRPYILRYVLFQDNSSHLPASAY	1440
Qy	1441	RKKSQVOESSHFLQGAKKNNLSIALITLLEMTDQDREVGSLGTSATNSVYKKKEVNTVLP	1500
Dp	1441	RKKSQVOESSHFLQGAKKNNLSIALITLLEMTDQDREVGSLGTSATNSVYKKKEVNTVLP	1500

[illegible]

XX	plasma proteases; thrombin; immunogen; antibody; haemophiliac; therapy;
XX	proteolytic cleavage.
XX	
XX	Homo sapiens.
XX	
XX	synthetic.
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XX	Key
XX	Location/Qualifiers
XX	Peptide
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XX	/note= "heavy chain fragment"
XX	Misc-difference
XX	1664
XX	/note= "inserted residue"
XX	Region
XX	1669..2351
XX	/note= "light chain fragment"
XX	Domain
XX	760..1668
XX	/note= "B domain"
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XX	W09J03195-A1.
XX	
XX	30-JAN-1997.
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XX	09-JUL-1996;
XX	96WO-US11444.
XX	
XX	11-JUL-1995;
XX	95US-0001025.
XX	
XX	(CHIR ) CHIRON CORP.
XX	
XX	Cohen FE, Hung DT, Innis M;
XX	
XX	WPI; 1997-119050/21.
XX	
XX	Factor VIII:C analog modified adjacent to a non-activating Arg
XX	residue, used in the treatment of haemophiliacs, by improvement of
XX	haemostasis
XX	
XX	Claim 31: Page -: 90pp; English.
XX	
XX	AA011330-W11472 represent active Factor VIII:C analogues of the
XX	invention. These sequences were created by mutating the wild type Factor
XX	VIII:C coding sequence (see AA051557) using mutagenic primers. The
XX	analogues comprise a native Factor VIII:C polypeptide modified at a site
XX	adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
XX	participle is created. Factor VIII:C is a large glycoprotein that
XX	participates in the blood coagulation cascade that ultimately converts
XX	soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
XX	deficiency in Factor VIII:C is responsible for haemophilia A, which is an
XX	X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
XX	activated by plasma proteases, such as thrombin. During activation the
XX	mature polypeptide is cleaved to generate heavy and light chain fragments
XX	that are further cleaved. Complexes of two or more of the analogues,
XX	nucleic acids and vectors encoding them may be used alone or in
XX	conjunction with each other, for the prevention or treatment of active
XX	Factor VIII:C deficiency in a mammal. The analogues may be used as
XX	immunogens to raise antibodies, and in the treatment of haemophiliacs, by
XX	improvement of haemostasis. The analogues are resistant to proteolytic
XX	cleavage and display increased plasma half-life. They may be administered
XX	at lower dosages and by different modes of administration.
XX	
XX	Sequence 2352 AA:
XX	
XX	Query Match 99.9%; Score 12407.5; DB 18; Length 2352;
XX	Best Local Similarity 100.0%; Pred. NO. 0;
XX	Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1
XX	
XX	1 MOELSTCFCLCLRCFSNTRRYLGAVELSDWYMSDGLGELPVDARPPRVKSPFN 60
XX	
XX	1 MOELSTCFCLCLRCFSNTRRYLGAVELSDWYMSDGLGELPVDARPPRVKSPFN 60
XX	
XX	61 TGVVKKLLEFEEFDHLFNIAKPRPMWGLGPIQAEVYDVIVTLNMSHVSLSHAV 120

Dd	61	TSVYTKTLPLVEFDHLFNIAKPRPMKGLLGPLOAEVYDTVTITLKNAHSPIVSLAV	120
Qy	121	GVSYKASGEAEYDDOTSOREKEDDKVFPGSGHYYWOLAKENGPMSADPLCTJYSYLH	180
Dd	121	GVSYKASGEAEYDDOTSOREKEDDKVFPGSGSHYYWOLAKENGPMSADPLCTJYSYLH	180
Qy	181	VDLVJDLNSGIGALLVYCEBGSLAKERQOTLHFFILFLFVPEDEKSMHSETKNSLMQDND	240
Dd	181	VDLVJDLNSGIGALLVYCEBGSLAKERQOTLHFFILFLFVPEDEKSMHSETKNSLMQDND	240
Qy	241	AASARMPKMTYGVYKNSLPGJLGCGRKSYVWHYIGMGTPEVHSJFLEGTFLVARNH	300
Dd	241	AASARMPKMTYGVYKNSLPGJLGCGRKSYVWHYIGMGTPEVHSJFLEGTFLVARNH	300
Qy	301	ROASLSEIPFLFAOTLLMDJGOFLECHSSHODMGAEAVKYKDSPEEOLRKNNE	360
Dd	301	ROASLSEIPFLFAOTLLMDJGOFLECHSSHODMGAEAVKYKDSPEEOLRKNNE	360
Qy	361	EADYDDDLTDEMDVYREDNDSPSFIQIRSAKKNPKTYVHTIAAEEEDMYAPLYA	420
Dd	361	EADYDDDLTDEMDVYREDNDSPSFIQIRSAKKNPKTYVHTIAAEEEDMYAPLYA	420
Qy	421	PDORSKSOYLNNGPORIGRKYKARFMAATYDETFTKRAIDHESGILGFLLYGEVDTL	480
Dd	421	PDORSKSOYLNNGPORIGRKYKARFMAATYDETFTKRAIDHESGILGFLLYGEVDTL	480
Qy	481	LIIFFKNQASRPYNYPPGJTDVRLPYSRLLPKGKHLKOFILPELFEFKKMYVEDBP	540
Dd	481	LIIFFKNQASRPYNYPPGJTDVRLPYSRLLPKGKHLKOFILPELFEFKKMYVEDBP	540
Qy	541	TSQDRCLTRYSSFYVMRERDLSGLJGFLILICYKSYOORONQMSKKNVLLFVPEPE	600
Dd	541	TSQDRCLTRYSSFYVMRERDLSGLJGFLILICYKSYOORONQMSKKNVLLFVPEPE	600
Qy	601	NNSWVLTEINIOREFPNAGYOUEDEPFOASIMHSTNGYFDSLOLSYCHAEVAYYIIS	660
Dd	601	NNSWVLTEINIOREFPNAGYOUEDEPFOASIMHSTNGYFDSLOLSYCHAEVAYYIIS	660
Qy	661	IGAQTDPLSVFSGCYTFKHKMYEDTTLTLPFSGETVEMSNBPGJLILCHNSDRNNG	720
Dd	661	IGAQTDPLSVFSGCYTFKHKMYEDTTLTLPFSGETVEMSNBPGJLILCHNSDRNNG	720
Qy	721	MPALIKVSSCKKNGDYEDSEYEDISAILSKNNALTEPFSFONSRRHSTROKOFNATTI	780
Dd	721	MPALIKVSSCKKNGDYEDSEYEDISAILSKNNALTEPFSFONSRRHSTROKOFNATTI	780
Qy	781	PENDLEKTDPMFAIRPMPKIONVSSDMLLROSPRPHGSLSDLOEAKYETFDSDPS	840
Dd	781	PENDLEKTDPMFAIRPMPKIONVSSDMLLROSPRPHGSLSDLOEAKYETFDSDPS	840
Qy	841	PGADISNNNSLSEMHHPOLHHSGDMVTPESSGLOLMEKIGTAAATELAKIDFVYSST	900
Dd	841	PGADISNNNSLSEMHHPOLHHSGDMVTPESSGLOLMEKIGTAAATELAKIDFVYSST	900
Qy	901	NNNLITSTIPSDNLAAGTDNTSSLGPPSPVHYDSOLOTLTFGKSSPLTFESGJLSLEE	960
Dd	901	NNNLITSTIPSDNLAAGTDNTSSLGPPSPVHYDSOLOTLTFGKSSPLTFESGJLSLEE	960
Qy	961	NNDSKLTESGJLANSOESSMGKNVSTESGRLFGKGAHAPALLTJDNALFKVYSISLTKN	1020
Dd	961	NNDSKLTESGJLANSOESSMGKNVSTESGRLFGKGAHAPALLTJDNALFKVYSISLTKN	1020
Qy	1021	KTSNNSAATNRKTHIDGSPILLINSGSWONILTSDEPFEKKYPLIHDRLMDKNATALL	1080
Dd	1021	KTSNNSAATNRKTHIDGSPILLINSGSWONILTSDEPFEKKYPLIHDRLMDKNATALL	1080
Qy	1081	NHMSKNTTSSKNMAYOQKEGPDPDQANDMSFFKMLLPESARWIOETHGKNSLNSG	1140
Dd	1081	NHMSKNTTSSKNMAYOQKEGPDPDQANDMSFFKMLLPESARWIOETHGKNSLNSG	1140
Qy	1141	OGSPKOLVSLGPEKSYEGONFLSEKKNVYVVGGEFTYKQVGLKEVYPPSSRNJFLTNLDN	1200
Dd	1141	OGSPKOLVSLGPEKSYEGONFLSEKKNVYVVGGEFTYKQVGLKEVYPPSSRNJFLTNLDN	1200

QY	1201	LHEHNTNHOEKKIOEIEIEKKEETLJOENVYLPOIHTVTGKTKMKNLFIILSTBRONVGSYD	1260
DB	1201	LHEHNTNHOEKKIOEIEIEKKEETLJOENVYLPOIHTVTGKTKMKNLFIILSTBRONVGSYD	1260
QY	1261	GAYAPYLODFRSLNDSTNRTKHTTAHFSKKEEENLEGLNQTKOQIYERACTTRISPT	1320
DB	1261	GAYAPYLODFRSLNDSTNRTKHTTAHFSKKEEENLEGLNQTKOQIYERACTTRISPT	1320
QY	1321	SOONFVOTSRKALQKQRLPLEETELEKRIIYDOSTQMSKMKHLPSTILOIDYNEKE	1380
DB	1321	SOONFVOTSRKALQKQRLPLEETELEKRIIYDOSTQMSKMKHLPSTILOIDYNEKE	1380
QY	1381	KGALIOSPLSDCIIRSHSIPQANRSPRLIAKXSSPSTRPYLTRVLFDONSSH.PAASY	1440
DB	1381	KGALIOSPLSDCIIRSHSIPQANRSPRLIAKXSSPSTRPYLTRVLFDONSSH.PAASY	1440
QY	1441	RKKDSGVDESSHFLQGAKKNNLSLAILLEMTGDQREYGLSGTSATNSVYKKVENTYLP	1500
DB	1441	RKKDSGVDESSHFLQGAKKNNLSLAILLEMTGDQREYGLSGTSATNSVYKKVENTYLP	1500
QY	1501	KPDLPTSGKVELLPKHITQKDLPTETSNQSPGHDLVYGSLQGTGATKMNDEANRP	1560
DB	1501	KPDLPTSGKVELLPKHITQKDLPTETSNQSPGHDLVYGSLQGTGATKMNDEANRP	1560
QY	1561	GKYPFLRATVATSSAKTSPKLLDPLANDNHTQIPIKREEMKSOEKSPEKTAFFKKDTIISL	1620
DB	1561	GKYPFLRATVATSSAKTSPKLLDPLANDNHTQIPIKREEMKSOEKSPEKTAFFKKDTIISL	1620
QY	1621	NACESNHAIAIINEGONKPEIEVTMAKQGRTRILCSQNPVLK-RHQREITRTTLQSDOE	1679
DB	1621	NACESNHAIAIINEGONKPEIEVTMAKQGRTRILCSQNPVLKRRHQREITRTTLQSDOE	1680
QY	1680	EIDYDPTISVEKKEDDIDYDEENQSPSPQKTRHETIAAVRLMDGMSSPHVLRN	1739
DB	1681	EIDYDPTISVEKKEDDIDYDEENQSPSPQKTRHETIAAVRLMDGMSSPHVLRN	1740
QY	1740	RAQSGSVPOFKVVOEFTDGSFTQPLYGELNEHLGLGPLYIAEVEDNINWTERNOAS	1799
DB	1741	RAQSGSVPOFKVVOEFTDGSFTQPLYGELNEHLGLGPLYIAEVEDNINWTERNOAS	1800
QY	1800	RPYSFYSSLISYEEDQROGAEPKRNFKVKNETKTYFMKVQJHMAPTKDEDFCKANAYESD	1859
DB	1801	RPYSFYSSLISYEEDQROGAEPKRNFKVKNETKTYFMKVQJHMAPTKDEDFCKANAYESD	1860
QY	1860	VDLEKDVHSGILGPLVCHNTNLPNPAHROVVOEFALFTIIPETKSWFTFENNERNCR	1919
DB	1861	VDLEKDVHSGILGPLVCHNTNLPNPAHROVVOEFALFTIIPETKSWFTFENNERNCR	1920
QY	1920	APCNIOEMEDPTFKENYRPHAINGYIMDTLPGLVMAQDORIRWYLLSMGSMENIHSHFSG	1979
DB	1921	APCNIOEMEDPTFKENYRPHAINGYIMDTLPGLVMAQDORIRWYLLSMGSMENIHSHFSG	1980
QY	1980	HVEVTAKKEEYKMAIYNLYPGVEFEVEMLPKAGIWRRECLIGBHLHAGMSTLFLVYSNK	2039
DB	1981	HVEVTAKKEEYKMAIYNLYPGVEFEVEMLPKAGIWRRECLIGBHLHAGMSTLFLVYSNK	2040
QY	2040	COTPLGMAAGHTRDPOITTAQOYGOMAPKLAIAHSSGSIINAMSGKPEPSIKYIDLAPMI	2099
DB	2041	COTPLGMAAGHTRDPOITTAQOYGOMAPKLAIAHSSGSIINAMSGKPEPSIKYIDLAPMI	2100
QY	2100	IHGIKTOGAROKFSSLYISQFIIMYSLDKCKMOTYRGNSGTGLTWPFQVNDSSGKIHNF	2159
DB	2101	IHGIKTOGAROKFSSLYISQFIIMYSLDKCKMOTYRGNSGTGLTWPFQVNDSSGKIHNF	2160
QY	2160	NPPIIARYIRLHPTIYRSTIRLMEIWMGCDLNSCIMPJGMSKSIISAQITASSYTTNPF	2219
DB	2161	NPPIIARYIRLHPTIYRSTIRLMEIWMGCDLNSCIMPJGMSKSIISAQITASSYTTNPF	2220
QY	2220	ATMSPSKARLHLOGSNAMRPOVNNKREMLQVDEOKTKATKGTGVTQOVKSLTSMVYEF	2279
DB	2221	ATMSPSKARLHLOGSNAMRPOVNNKREMLQVDEOKTKATKGTGVTQOVKSLTSMVYEF	2280

QY	2280	LISSSDGQHONTLFPONGKVKVFGNODSFTPVNSLDPPLLFYRLIRHPQSMVHQIALR	2335
DB	2281	LISSSDGQHONTLFPONGKVKVFGNODSFTPVNSLDPPLLFYRLIRHPQSMVHQIALR	2340
QY	2340	MEVLCGEADLX 2351	
DB	2341	MEVLCGEADLX 2352	
RESULT 36			
ID	AAW11439	standard; Protein; 2352 AA.	
XX			
AC	AAW11439;		
XX			
DE	20-NOV-1997	(first entry)	
XX			
DE	Active Factor VIII:C analogue residue 1646 P insertion.		
XX			
KW	Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;		
KM	fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;		
KW	plasma protease; thrombin; immunogen; antibody; haemophillic therapy;		
KW	proteolytic cleavage.		
OS	Homo sapiens.		
OS	Synthetic.		
XX			
PH	Key	Location/Qualifiers	
FT	Peptide	1..19	
FT	/note= "signal peptide"		
FT	Protein	20..2352	
FT	/note= "mature Factor VIII:C"		
FT	Region	20..1668	
FT	/note= "heavy chain fragment"		
FT	Misc-difference	1665	
FT	/note= "inserted residue"		
FT	Region	1669..2351	
FT	/note= "light chain fragment"		
FT	Domain	760..1668	
FT	/note= "B domain"		
PN	W09703195-A1.		
XX			
PD	30-JAN-1997.		
XX			
PF	09-JUL-1996;	96MO-US11444.	
XX			
PR	11-JUL-1995;	95US-0001025.	
XX			
PA	(CHIR ) CHIRON CORP.		
XX			
PI	Cohen FE, Hung DT, Innis M;		
XX			
DR	WPI; 1997-119050/11.		
XX			
PT	Factor VIII:C analog modified adjacent to a non-activating Arg		
PT	residue - used in the treatment of haemophillics, by improvement of		
PT	haemostasis		
PS	Claim 31; Page -; 90pp; English.		
XX			
CC	AAW11330-W11472 represent active Factor VIII:C analogues of the		
CC	invention. These sequences were created by mutating the wild type Factor		
CC	VIII:C coding sequence (see AAT51357) using mutagenic primers. The		
CC	analogues comprise a native Factor VIII:C polypeptide modified at a site		
CC	adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg		
CC	participates in the blood coagulation cascade that ultimately converts		
CC	soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A		
CC	deficiency in Factor VIII:C is responsible for haemophilia A, which is an		
CC	X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is		
CC	activated by plasma proteases, such as thrombin. During activation the		
CC	mature polypeptide is cleaved to generate heavy and light chain fragments		



that are further cleaved. Complexes of two or more of the analogues, nucleic acids and vectors encoding them may be used alone or in conjunction with each other, for the prevention or treatment of active Factor VIII:C deficiency in a mammal. The analogues may be used as immunogens to raise antibodies, and in the treatment of haemophiliacs, by improvement of haemostasis. The analogues are resistant to proteolytic cleavage and display increased plasma half-life. They may be administered at lower dosages and by different modes of administration.

SQ Sequence 2352 AA;

Query Match	99.9%;	Score 12407.5;	DB 18;	Length 2352;
Best Local Similarity	100.0%;	Pred. No. 0;		
Matches 2351;	Conservative 0;	Mismatches 0;	Indels 1;	Gaps 1;

Qy	1	MOLESTOFFCLILRCFSASTRRYLGAVELSMDWYOSIGELPVDAPFPRPKSPNN	60
Db	1	MOLESTOFFCLILRCFSASTRRYLGAVELSMDWYOSIGELPVDAPFPRPKSPNN	60
Qy	61	TSVYKKTLLFEVETDHLFNIAKPRPPMGLIPTQAEYDVIVITLKNMASHVSLAH	120
Db	61	TSVYKKTLLFEVETDHLFNIAKPRPPMGLIPTQAEYDVIVITLKNMASHVSLAH	120
Qy	121	GVSYMKASGEAYEDQSOKEKEDKVPGGSGSHYVQVLEKNGMADDPCLCTLYSLSH	180
Db	121	GVSYMKASGEAYEDQSOKEKEDKVPGGSGSHYVQVLEKNGMADDPCLCTLYSLSH	180
Qy	181	VDLYVDLNSGLIGLLYCPGSLAKKQTLAKTLLFAVPECKSWSEFKNSLMODR	240
Db	181	VDLYVDLNSGLIGLLYCPGSLAKKQTLAKTLLFAVPECKSWSEFKNSLMODR	240
Qy	241	AASARAMPKMTYNGVYNSRLPGLIGCHRSVYWHVIGMCTTPEVHSTIFLEGHTFLVRN	300
Db	241	AASARAMPKMTYNGVYNSRLPGLIGCHRSVYWHVIGMCTTPEVHSTIFLEGHTFLVRN	300
Qy	301	ROASLEISFPEPLAQTLLMDLGOFLTEFCHSHSHQHGMAYAYKVDSCPEEPOLRMKNN	360
Db	301	ROASLEISFPEPLAQTLLMDLGOFLTEFCHSHSHQHGMAYAYKVDSCPEEPOLRMKNN	360
Qy	361	EADYDDDLTDSENDYVREFDDNPSFIOINSVAKKPKTWHYIAAEBMDYAPLYLA	420
Db	361	EADYDDDLTDSENDYVREFDDNPSFIOINSVAKKPKTWHYIAAEBMDYAPLYLA	420
Qy	421	PDRSRKSOYLNGFORIGRKRYKKVAFMAVTEYFKTREAIOHESGILBPLLYGEBDGL	480
Db	421	PDRSRKSOYLNGFORIGRKRYKKVAFMAVTEYFKTREAIOHESGILBPLLYGEBDGL	480
Qy	481	LIIFKQASRPNIYPRGIDTWRPLXSRPLSPGYKHLKDPILLRGIFFYKKMTYVDEGP	540
Db	481	LIIFKQASRPNIYPRGIDTWRPLXSRPLSPGYKHLKDPILLRGIFFYKKMTYVDEGP	540
Qy	541	TKSDPRCLTRYYSFVNNERDLASGLIGBLLCYKESYDVRGNQIMSDRNYLFSVFE	600
Db	541	TKSDPRCLTRYYSFVNNERDLASGLIGBLLCYKESYDVRGNQIMSDRNYLFSVFE	600
Qy	601	NBSWYLTENIOEFLPNPAGVOLEDPEFOASNMHSINCYEFSIOJSLVCLHEVAWYLLS	660
Db	601	NBSWYLTENIOEFLPNPAGVOLEDPEFOASNMHSINCYEFSIOJSLVCLHEVAWYLLS	660
Qy	661	IGAOTDFLSVFPSGTYFKHKMYIEDTLLFPSSGCTYMSKENPGLMILGCINSFRRG	720
Db	661	IGAOTDFLSVFPSGTYFKHKMYIEDTLLFPSSGCTYMSKENPGLMILGCINSFRRG	720
Qy	721	MTALLKXSGCDNKGDYEDSYEDISAYLLSKNNAIEPRSPSONSRHSTROKONATTI	780
Db	721	MTALLKXSGCDNKGDYEDSYEDISAYLLSKNNAIEPRSPSONSRHSTROKONATTI	780
Qy	781	PENDIEKTPWFAHRTPMPKIQNVSSDMLMLRSPPHGLSISLDOEKATEYSDPS	840
Db	781	PENDIEKTPWFAHRTPMPKIQNVSSDMLMLRSPPHGLSISLDOEKATEYSDPS	840
Qy	841	PGALDSNNSISEMTHFRPOLHHSGDWTFPESGLOLRINELIGTAAATELKIDKXVST	900
Db	841	PGALDSNNSISEMTHFRPOLHHSGDWTFPESGLOLRINELIGTAAATELKIDKXVST	900

Db	841	PCADISNNLSIEBMTHFRPQLHSHGDWVFTPESSGLOLRINEKLGITTAATELAKIDFVYSST	900
Qy	901	NNULISTIPSNLAAGTDMNTSLGPPSPMVBHYDSQDLDTLTGKSSPLTESSGPLSLEE	960
Db	901	NNULISTIPSNLAAGTDMNTSLGPPSPMVBHYDSQDLDTLTGKSSPLTESSGPLSLEE	960
Qy	961	NNDSKILLEGGLANSQESGCKKNVSTRESSGATKGRRAGPLLTKNDALPKVYSISLTKTN	1020
Db	961	NNDSKILLEGGLANSQESGCKKNVSTRESSGATKGRRAGPLLTKNDALPKVYSISLTKTN	1020
Qy	1021	KTSNNSATRKTHIDGSPSLIENSPLYWONILSDTEEFKKVYPLIHDBMLDKNATRLH	1080
Db	1021	KTSNNSATRKTHIDGSPSLIENSPLYWONILSDTEEFKKVYPLIHDBMLDKNATRLH	1080
Qy	1081	NHNSKNTSSKKNMEVQOKKEGPIPPAOQPDMSFFKMLFPEASRWIOPTHGKNSLNSG	1140
Db	1081	NHNSKNTSSKKNMEVQOKKEGPIPPAOQPDMSFFKMLFPEASRWIOPTHGKNSLNSG	1140
Qy	1141	OGSPKQOVLVSIGPEKSVBQONFLSEKKVVYVGKGETKYGVGLKEVFPSSNPLFTIMLN	1200
Db	1141	OGSPKQOVLVSIGPEKSVBQONFLSEKKVVYVGKGETKYGVGLKEVFPSSNPLFTIMLN	1200
Qy	1201	LHNNHTNHNQEKIOEIEIEKKEETLLIOENVVLPQIHTVYGTKNPMKNLFLSTRONBESYD	1260
Db	1201	LHNNHTNHNQEKIOEIEIEKKEETLLIOENVVLPQIHTVYGTKNPMKNLFLSTRONBESYD	1260
Qy	1261	GATAPVLOPRLNSTNRKTKHNAHSSKSGEENLEGNOTKQIYEVKVACTRISPT	1320
Db	1261	GATAPVLOPRLNSTNRKTKHNAHSSKSGEENLEGNOTKQIYEVKVACTRISPT	1320
Qy	1321	SOONFYVORSKRALQOPLPLEETELEKRIIVDSTONSKMMKHLFSTLTQIDYENKE	1380
Db	1321	SOONFYVORSKRALQOPLPLEETELEKRIIVDSTONSKMMKHLFSTLTQIDYENKE	1380
Qy	1381	KGATOSPISDCITRSHSIPQANSPLPIAKVSSPISPIPLTYLTVLQODNSHLPAASY	1440
Db	1381	KGATOSPISDCITRSHSIPQANSPLPIAKVSSPISPIPLTYLTVLQODNSHLPAASY	1440
Qy	1441	RKSDGVQESSHFLQAGAKNNLSIALITLEMTGDQREVSGLSGTSATNSVYTKKYENYVLP	1500
Db	1441	RKSDGVQESSHFLQAGAKNNLSIALITLEMTGDQREVSGLSGTSATNSVYTKKYENYVLP	1500
Qy	1501	KPDLPKTSGVVELLPVNIYOKDLPPEYTSNGSPGHLDIVEGSLQGTGEGAIKNNEANRP	1560
Db	1501	KPDLPKTSGVVELLPVNIYOKDLPPEYTSNGSPGHLDIVEGSLQGTGEGAIKNNEANRP	1560
Qy	1561	GVDFPLVATESSAKTPEKLDPLANDNHYTQIPREKMSQOKSPEKTAFFKKDTILSL	1620
Db	1561	GVDFPLVATESSAKTPEKLDPLANDNHYTQIPREKMSQOKSPEKTAFFKKDTILSL	1620
Qy	1621	NACSNNAIAINIEGONKPEIEVYNAKQGRTERLCSONPVLKR-HQREITRTTLQSDOE	1679
Db	1621	NACSNNAIAINIEGONKPEIEVYNAKQGRTERLCSONPVLKR-HQREITRTTLQSDOE	1680
Qy	1680	EIDYDDTISYEMKKKEPDLYDEDEMOGRSQOKTTHYFLAAVERLMDVGMSSPHVLRN	1739
Db	1681	EIDYDDTISYEMKKKEPDLYDEDEMOGRSQOKTTHYFLAAVERLMDVGMSSPHVLRN	1740
Qy	1740	RAQSGSVPOKRVVFOEFTDGSFTQPLYRGELNHLGLCPYIRAEVDNIWYTRRNQAS	1799
Db	1741	RAQSGSVPOKRVVFOEFTDGSFTQPLYRGELNHLGLCPYIRAEVDNIWYTRRNQAS	1800
Qy	1800	RPYSPYSLSIYEEDROGAGBPRKKNFVNPENETKTYIPMKVOHNHAAPKDKDFDCKAANAYS	1859
Db	1801	RPYSPYSLSIYEEDROGAGBPRKKNFVNPENETKTYIPMKVOHNHAAPKDKDFDCKAANAYS	1860
Qy	1860	VDLEKDVHSGILGPLYVCHTNTLNPAGROYTVOEFALEFTFDETKSWYFTENNERCKR	1919
Db	1861	VDLEKDVHSGILGPLYVCHTNTLNPAGROYTVOEFALEFTFDETKSWYFTENNERCKR	1920
Qy	1920	APCNQIOMDPPREKENRPHANINGYIMDTLPGLVYMAOORLRWMLTMSGNSNENHSHIRFSG	1979
Db	1921	APCNQIOMDPPREKENRPHANINGYIMDTLPGLVYMAOORLRWMLTMSGNSNENHSHIRFSG	1980



Oy	1980	HYFTYRKKEEYKALNLNYPGFEFEVEMLPKSGKIMRVBCLIGHLHAGKSTLEFLYYSNK	2039
Dd	1981	HYFTYRKKEEYKALNLNYPGFEFEVEMLPKSGKIMRVBCLIGHLHAGKSTLEFLYYSNK	2040
Oy	2040	COTPLGMAASHITDPOITASGOYQGMAPKIALRHYSGSINMASTKEPFSWIKYDLAPFI	20999
Dd	2041	COTPLGMAASHITDPOITASGOYQGMAPKIALRHYSGSINMASTKEPFSWIKYDLAPFI	21000
Oy	2100	IHGKTKGANKRFSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFEGNVDSGICKANIF	21599
Dd	2101	IHGKTKGANKRFSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFEGNVDSGICKANIF	21600
Oy	2160	NPPIIARIYIRLHPHTHSIKSTLRMBELMGCDLNCSCNPILGMEKASIAISAOITASSYPTNMF	22199
Dd	2161	NPPIIARIYIRLHPHTHSIKSTLRMBELMGCDLNCSCNPILGMEKASIAISAOITASSYPTNMF	22200
Oy	2220	ATWSPSKARLHLGGRSNAMRPVNNPKEMQLQVDFOKTKYVTGVTGQVKSILRSMYVKEF	22799
Dd	2221	ATWSPSKARLHLGGRSNAMRPVNNPKEMQLQVDFOKTKYVTGVTGQVKSILRSMYVKEF	22800
Oy	2280	LISSSGOGHOMTLEFPNGKVKYFEGGNDSTPPVNSLDPILLTYLRLIHQOSMVDIAR	23399
Dd	2281	LISSSGOGHOMTLEFPNGKVKYFEGGNDSTPPVNSLDPILLTYLRLIHQOSMVDIAR	23400
Oy	2340	MEVLGCEADPLY 2351	
Dd	2341	MEVLGCEADPLY 2352	
RESULT 37			
AAWII442	AAWII442	standard; Protein; 2352 AA.	
AAWII442	AAWII442		
AC	AAWII442		
XX	20-NOV-1997	(first entry)	
DT	Active Factor VIII:C analogue residue 1644 F/E/P insertion.		
XX			
KW	Factor VIII:C analogue; glycoprotein; blood coagulation cascade; fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis; plasma protease; thrombin; immunogen; antibody; haemophilic; therapy; proteolytic cleavage.		
KW			
XX	Homo sapiens.		
OS	Synthetic.		
XX			
FT	Key	Location/Qualifiers	
FT	Peptide	1..19	
FT	Protein	/note="signal peptide"	
FT	Region	20..2352	
FT	Region	/note="mature Factor VIII:C"	
FT	Modified-site	20..1668	
FT		/note="heavy chain fragment"	
FT		1663	
FT	Region	/label="Phe, Glu, Pro	
FT		/note="inserted residue"	
FT	Domain	1669..2351	
FT		/note="light chain fragment"	
FT		760..1668	
FT		/note="B domain"	
XX	NO9703195-A1.		
XX			
XX	30-JAN-1997.		
XX	09-JUL-1996;	96WO-USI1444.	
XX	11-JUL-1995;	95US-0001025.	
XX	(CHIR ) CHIRON CORP.		

PI	Cohen Fe,	Hung DT,	InnIs M;
XX	DR	WPI,	1997-119050/11.
PT	Factor VIII:C analog modified adjacent to a non-activating Arg residue used in the treatment of haemophilias, by improvement of haemostasis		
PS	Claim 32:	Page -:	90pp: English.
CC	AAAM1330-W1472 represent active Factor VIII:C analogues of the invention. These sequences were created by mutating the wild type Factor VIII:C coding sequence (see AAH51357) using mutagenic primers. The analogues comprise a native Factor VIII:C polypeptide modified at a site adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg peptide is created. Factor VIII:C is a large glycoprotein that participates in the blood coagulation cascade that ultimately converts soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A deficiency in Factor VIII:C is responsible for haemophilia A, which is an X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is activated by plasma proteases, such as thrombin. During activation the mature polypeptide is cleaved to generate heavy and light chain fragments that are further cleaved. Complexes of two or more of the analogues, nucleic acids and vectors encoding them may be used alone or in conjunction with each other, for the prevention or treatment of active Factor VIII:C deficiency in a mammal. The analogues may be used as immunogens to raise antibodies, and in the treatment of haemophilias, by improvement of haemostasis. The analogues are resistant to proteolytic cleavage and display increased plasma half-life. They may be administered at lower dosages and by different modes of administration.		
XX	Sequence	2352 AA:	
QY	Query Match	99.9%; Score 12407.5; DB 18; Length 2352;	
Dx	Best Local Similarity	100.0%; Pred. No. 0;	
Mt	Matches 2351:	Conservative 0; Mismatches 0; Indels 1; Gaps 1	
Oy	1 MOELSTCFEFLRCFSATRRYYLGAVELSMDDMOGLPVDARFPRYPKSPEN 60		
Dd	1 MOELSTCFEFLRCFSATRRYYLGAVELSMDDMOGLPVDARFPRYPKSPEN 60		
Oy	61 TSVYKKTLPEFTDLFIAPRPPMGLGPIAEEYDVTITLNMAHPVLSAHV 120		
Dd	61 TSVYKKTLPEFTDLFIAPRPPMGLGPIAEEYDVTITLNMAHPVLSAHV 120		
Oy	121 GYSWKASGEAEFDOTSOREEDDKYPPGSHIYYOVLKENGMSADPLCLTLYSLHS 180		
Dd	121 GYSWKASGEAEFDOTSOREEDDKYPPGSHIYYOVLKENGMSADPLCLTLYSLHS 180		
Oy	181 VDLVKDINSGLIGALLVCRESSLAKEKTOTLIHKFILFAVEDEGKSWHSSETKNSLMODRD 240		
Dd	181 VDLVKDINSGLIGALLVCRESSLAKEKTOTLIHKFILFAVEDEGKSWHSSETKNSLMODRD 240		
Oy	241 AASARAFPKMHITNGVYNSTRLGLLGCHRKRSVYWHVIGMTREPHNSTFLDGHTFLVRNH 300		
Dd	241 AASARAFPKMHITNGVYNSTRLGLLGCHRKRSVYWHVIGMTREPHNSTFLDGHTFLVRNH 300		
Oy	301 ROASTLEISPIETFAOTLLMDAGOFLECHNISHOHDBEAUVKVDSCEPEPOLRMKNNE 360		
Dd	301 ROASTLEISPIETFAOTLLMDAGOFLECHNISHOHDBEAUVKVDSCEPEPOLRMKNNE 360		
Oy	361 EAEVDDDLTDSEMDVVRTPDNDNSPFIOIRSVAKKHPTWNHYIAAEEEDMDYAPLVYA 420		
Dd	361 EAEVDDDLTDSEMDVVRTPDNDNSPFIOIRSVAKKHPTWNHYIAAEEEDMDYAPLVYA 420		
Oy	421 PDDBSKYQVYLANGPORIGRIKKYKKAEMAYNDEFPTREAOIHSGILGLYEVDLT 480		
Dd	421 PDDBSKYQVYLANGPORIGRIKKYKKAEMAYNDEFPTREAOIHSGILGLYEVDLT 480		
Oy	481 LTFEKNASRPYNIYHGTTIDRPLYSRLPKGYKLKORPLPGELFKMYTVYEDGP 540		
Dd	481 LTFEKNASRPYNIYHGTTIDRPLYSRLPKGYKLKORPLPGELFKMYTVYEDGP 540		

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721 MTALLKVSCKDNKTG DYEDSYEDISAYLLSKNNAIEPRSFQNSRHPSTKOKOFNATYI 780  
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781 PENDIEKTPWFARHTPMPKITIONVSSDLM.L.RQSPTRHGLSLDLOEAKYETFSDDPS 840  
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841 PGALDSNNLSLEMTHRPQLHSGDMVTPBSGLQRLNEKLTCTAATELKLDKXYSST 900  
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1321 SOONVTOORSKRALKOFRLPLETELEKRIIVDOTSTOMSKMKHLTPSTLTOIDYENKE 1380  
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1381 KGATOSP.LSDCLTRKSHSIPQANRSP.LPIAVSSP.SIRIYTLRVLRODNSHL.PASV 1440  
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2340 MEVLGCEA.DQ.LY 2351  
2340 MEVLGCEA.DQ.LY 2351  
2341 MEVLGCEA.DQ.LY 2352  
2341 MEVLGCEA.DQ.LY 2352

RESULT 38  
AA011447  
ID AA011447 standard; Protein; 2352 AA.  
XX  
AC AA011447;  
XX  
DT 20-NOV-1997 (first entry)  
XX  
DE Active Factor VIII:C analogue residue 1648 P insertion.  
XX  
KW Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;  
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KW plasma protease; thrombin; immunogen; antibody; haemophilia; therapy;  
KW proteolytic cleavage.  
XX  
OS Homo sapiens.  
OS  
OS Synthetic.  
XX  
FH key  
FT 1..19 Location/Qualifiers  
FT Peptide  
FT /note= "signal peptide"

Protein 20..2352  
/note= "mature Factor VIII:C"  
Region 20..1668  
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/note= "inserted residue"  
Region 1669..2351  
/note= "light chain fragment"  
Domain 760..1668  
/note= "B domain"

NO9703195-A1.  
30-JAN-1997.  
09-JUL-1996; 96MO-US11444.  
11-JUL-1995; 95US-0001025.  
(CHIR ) CHIRON CORP.  
Cohen FE, Hung DT, Innis M;  
WPI; 1997-119050/11.

Factor VIII:C analog modified adjacent to a non-activating Arg  
residue - used in the treatment of haemophiliacs, by improvement of  
haemostasis

Claim 33; Page -: 90pp; English.

AA11330-W11472 represent active Factor VIII:C analogues of the  
invention. These sequences were created by mutating the wild type Factor  
VIII:C coding sequence (see AA151357) using mutagenic primers. The  
analogues comprise a native Factor VIII:C polypeptide modified at a site  
adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
dipeptide is created. Factor VIII:C is a large glycoprotein that  
participates in the blood coagulation cascade that ultimately converts  
soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
activated by plasma proteases, such as thrombin. During activation the  
mature polypeptide is cleaved to generate heavy and light chain fragments  
that are further cleaved. Complexes of two or more of the analogues,  
nucleic acids and vectors encoding them may be used alone or in  
conjunction with each other, for the prevention or treatment of active  
Factor VIII:C deficiency in a mammal. The analogues may be used as  
immunogens to raise antibodies, and in the treatment of haemophiliacs, by  
improvement of haemostasis. The analogues are resistant to proteolytic  
cleavage and display increased plasma half-life. They may be administered  
at lower dosages and by different modes of administration.

Sequence 2352 AA;

Query Match 99.96; Score 12407.5; DB 18; Length 2352;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

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DB 61 TSVVYKKTLEVEFTDHLFNIAKRPWMGLGPTIOAEVDVTVITLKMASHPSLAHV 120  
QY 61 TSVVYKKTLEVEFTDHLFNIAKRPWMGLGPTIOAEVDVTVITLKMASHPSLAHV 120  
DB 61 TSVVYKKTLEVEFTDHLFNIAKRPWMGLGPTIOAEVDVTVITLKMASHPSLAHV 120  
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DB 121 GSVYKASGEAYDDOTSOREKEDKVPFGSGSHYVWQVLKENGPMASDPLCLTYSYLSH 180  
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DB 241 AASARAMPKMHVNGVYVNSRLPGLIGCHRRKSVYVWVHVGNGTTPREVHSIFLEGHTFLVRNH 300  
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DB 601 NRSWLTENIQRFLPAPACVOLDEPFOASNIHNSINGYVPSDLSYCLAEVAYWTIIS 660  
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DB 661 IGAOTDFLSVFFSGYFHKHMYEDTTLTPFSGETVFMKSNPGLMTLGCNHSDFRNKG 720  
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DB 901 SNNLITIPSDNLAAGTDNTSSIGPSPVHYDSQDITLFGKSSPLTESGCLSLSEE 960  
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DB 1681 EIDYDDTISVEMKKEPDIYDEENQSPRSFOKTRHYETAAVERLMDYGMSPPHYLRN 1740
QY 1740 RAQSGSVPOFKKVVFOEFDGFTOPILRGALNHGLGLPTRYRAVEDNINMTFRQAS 1799
DB 1741 RAQSGSVPOFKKVVFOEFDGFTOPILRGALNHGLGLPTRYRAVEDNINMTFRQAS 1800
QY 1800 RPYSTYSSLSIYEBEDORQAGAEPRKNFVKNPNETKTYFKVOHMAPTKDEPCKAMAYFSD 1859
DB 1801 RPYSTYSSLSIYEBEDORQAGAEPRKNFVKNPNETKTYFKVOHMAPTKDEPCKAMAYFSD 1860
QY 1860 VDLEKDVHSLIGLPLVCHNTLNPAGROYTVOEFALFTIDETKSYFENNERNCR 1919
DB 1861 VDLEKDVHSLIGLPLVCHNTLNPAGROYTVOEFALFTIDETKSYFENNERNCR 1920
QY 1920 APCNTQMEDPTFKENRPFHAINGYIMDTLPGVMAOQORIRKWLILSMGSNENIHSIHSG 1979
DB 1921 APCNTQMEDPTFKENRPFHAINGYIMDTLPGVMAOQORIRKWLILSMGSNENIHSIHSG 1980
QY 1980 HVEFYRKKKEEKMAALYNLYPGVFETVEMLPKAGIMVEECLIGEHLHAQSTLEFLVYSNK 2039
DB 1981 HVEFYRKKKEEKMAALYNLYPGVFETVEMLPKAGIMVEECLIGEHLHAQSTLEFLVYSNK 2040
QY 2040 COTPLGMAHSHIRFQITASGOYQOMAPKLARLHYSISINAMSTKEPFEMIVDLAPMI 2099
DB 2041 COTPLGMAHSHIRFQITASGOYQOMAPKLARLHYSISINAMSTKEPFEMIVDLAPMI 2100
QY 2100 IHCITQAGAROKFESSLYISOFILMYSLDGKMOYTRCNSGTCLAMFPGVDSGKKNHIF 2159
DB 2101 IHCITQAGAROKFESSLYISOFILMYSLDGKMOYTRCNSGTCLAMFPGVDSGKKNHIF 2160
QY 2160 NPPIIARYIRLHPHYSIRSTLMELMCDLNSCMBPLGEMSAISDAQITASSYFTNMF 2219
DB 2161 NPPIIARYIRLHPHYSIRSTLMELMCDLNSCMBPLGEMSAISDAQITASSYFTNMF 2220
QY 2220 ATWSPSKARLHLOGRSNAAMPPOVNNPKEMLOYDQOKMKTKYTGTTQGVSLTTSYVEEF 2279
DB 2221 ATWSPSKARLHLOGRSNAAMPPOVNNPKEMLOYDQOKMKTKYTGTTQGVSLTTSYVEEF 2280
QY 2280 LISSSQDGHQWTLFPGNGKVKYFQGNQDSFTPVVNSLDPPLLTRYLRHPOSWHQIALR 2339
DB 2281 LISSSQDGHQWTLFPGNGKVKYFQGNQDSFTPVVNSLDPPLLTRYLRHPOSWHQIALR 2340
QY 2340 MEVLGCEAQDLY 2351
DB 2341 MEVLGCEAQDLY 2352

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RESULT 39
AA011450
ID AA011450 standard; Protein; 2352 AA.
XX
AC AA011450;
XX
DT 20-NOV-1997 (first entry)
XX
DE Active Factor VIII:C analogue residue 1649 P insertion.
XX
KW Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;
XX proteolytic cleavage.
OS Homo sapiens.
XX Synthetic.
XX
FH Key Location/Qualifiers
FH Peptide 1..19
FH Protein /note="signal peptide"
FH Region /note="mature Factor VIII:C"
FH Region /note="heavy chain fragment"
FH Misc-difference /note="1668
FH Region /note="inserted residue"
FH Region /note="1659..2351
FH Domain /note="light chain fragment"
FH Domain /note="760..1667
FH Domain /note="B domain"
XX
PN WO9703195-A1.
XX
PD 30-JAN-1997.
XX
PF 09-JUL-1996; 96WO-US1144.
XX
PR 11-JUL-1995; 95US-0001025.
XX
PA (CHIR ) CHIRON CORP.
XX
PI Cohen FE, Hung DT, Innis M;
XX
DR WPI: 1997-119050/11.
XX
PT Factor VIII:C analog modified adjacent to a non-activating Arg
PT residue - used in the treatment of haemophilias, by improvement of
PT haemostasis
XX
PS Claim 33; Page 7; 90pp; English.
XX
AA011330-W11472 represent active Factor VIII:C analogues of the
XX invention. These sequences were created by mutating the wild type Factor
XX VIII:C coding sequence (see AA015157) using mutagenic primers. The
XX analogues comprise a native Factor VIII:C polypeptide modified at a site
XX adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
XX dipeptide is created. Factor VIII:C is a large glycoprotein that
XX participates in the blood coagulation cascade that ultimately converts
XX soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
XX deficiency in Factor VIII:C is responsible for haemophilia A, which is an
XX X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
XX activated by plasma proteases, such as thrombin. During activation the
XX mature polypeptide is cleaved to generate heavy and light chain fragments
XX that are further cleaved. Complexes of two or more of the analogues,
XX nucleic acids and vectors encoding them may be used alone or in
XX conjunction with each other, for the prevention or treatment of active
XX Factor VIII:C deficiency in a mammal. The analogues may be used as
XX immunogens to raise antibodies, and in the treatment of haemophilias, by
XX improvement of haemostasis. The analogues are resistant to proteolytic
XX cleavage and display increased plasma half-life. They may be administered
XX at lower dosages and by different modes of administration.
XX

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50	Sequence	2352 AA;	
	Query Match	99.9%; Score 12407.5; DB 18; Length 2352;	
	Best Local Similarity	100.0%; Pred. No. 0;	
	Matches 2351;	Conservative 0; Mismatches 0; Indels 1; Gaps 1;	
Oy	1	MOELSTCFELCLRCFSATRRYYLGAVELSMDYQOSDLGELPYDARPPRPVKSPFPN	60
Db	1	MOELSTCFELCLRCFSATRRYYLGAVELSMDYQOSDLGELPYDARPPRPVKSPFPN	60
Oy	61	TSVYVKKTLFEVEFTDLFNIAKPRPMGLGPTIOAEVYDVVITLKNMASHPSLHAY	120
Db	61	TSVYVKKTLFEVEFTDLFNIAKPRPMGLGPTIOAEVYDVVITLKNMASHPSLHAY	120
Oy	121	GVSYWKASEGAEVDDOTSOREKEDDKVPGSGSHYYMNYLKEGMPASDPCLYSLSH	180
Db	121	GVSYWKASEGAEVDDOTSOREKEDDKVPGSGSHYYMNYLKEGMPASDPCLYSLSH	180
Oy	181	VDLVKDLNSGLIGALLVCREGSLAEKQTOLHKFLLFAVDEGKSMHSETKNSLMODRD	240
Db	181	VDLVKDLNSGLIGALLVCREGSLAEKQTOLHKFLLFAVDEGKSMHSETKNSLMODRD	240
Oy	241	AASARAMPKMTVNGVYVNRSLPGLIGCHRSYVWHVIGMGTPEVHSIFLEGHTFLVNH	300
Db	241	AASARAMPKMTVNGVYVNRSLPGLIGCHRSYVWHVIGMGTPEVHSIFLEGHTFLVNH	300
Oy	301	ROASLEISPTTFAAGTLLMDLGOFPLCGHSHQHMGMAVYKVDSCEEPQLMKMNE	360
Db	301	ROASLEISPTTFAAGTLLMDLGOFPLCGHSHQHMGMAVYKVDSCEEPQLMKMNE	360
Oy	361	EAEDYDDDLTDEMDVVRDDDNSSPFIQIRSVAKKHPKTMVHYIAEEDMDYAPLVLA	420
Db	361	EAEDYDDDLTDEMDVVRDDDNSSPFIQIRSVAKKHPKTMVHYIAEEDMDYAPLVLA	420
Oy	421	PPDRSYKSOYLNNGPORGKRYKRYFMAAYTDEFKTRREALIOHESGILLPLLYGVGDTL	480
Db	421	PPDRSYKSOYLNNGPORGKRYKRYFMAAYTDEFKTRREALIOHESGILLPLLYGVGDTL	480
Oy	481	LIIFKNQASRPYNYTPHGITDVAPLYSRPLKGYKHLKDPPLPGEIFYKKTVYVEDGP	540
Db	481	LIIFKNQASRPYNYTPHGITDVAPLYSRPLKGYKHLKDPPLPGEIFYKKTVYVEDGP	540
Oy	541	TKSDPRCLTRYSSFVNMERDLASGLIPLLICYKESVDORGNQIMSDKRNVIIFYEDE	600
Db	541	TKSDPRCLTRYSSFVNMERDLASGLIPLLICYKESVDORGNQIMSDKRNVIIFYEDE	600
Oy	601	NRSWYLTENIORFLPNPAGVQLEDPFOASNMHSTINGVYFDSLQVLCHEVAWYTLIS	660
Db	601	NRSWYLTENIORFLPNPAGVQLEDPFOASNMHSTINGVYFDSLQVLCHEVAWYTLIS	660
Oy	661	IGAOTDFLSVFSGTTFKHKMYEDTLFLPPSGEIVFMSMENPGLIWLIGCHNSDFNRNG	720
Db	661	IGAOTDFLSVFSGTTFKHKMYEDTLFLPPSGEIVFMSMENPGLIWLIGCHNSDFNRNG	720
Oy	721	MTALLKVSQCDKNTGDYEDSYEDISAYLLSKNNAIEPRSFSONSRHPTROKQONATTI	780
Db	721	MTALLKVSQCDKNTGDYEDSYEDISAYLLSKNNAIEPRSFSONSRHPTROKQONATTI	780
Oy	781	PENDIEKTDPMFAHRTPMKIOWSSDLMILKOSPTPHGSLSDLOAKETYSDDPS	840
Db	781	PENDIEKTDPMFAHRTPMKIOWSSDLMILKOSPTPHGSLSDLOAKETYSDDPS	840
Oy	841	PGAIDSNNSISEMTHFHPOLHSGDMVTPESGQLOLRINEKLTJTAATLKLKLDPKVYST	900
Db	841	PGAIDSNNSISEMTHFHPOLHSGDMVTPESGQLOLRINEKLTJTAATLKLKLDPKVYST	900
Oy	901	SNNLISTIPSDNLAAAGDNTSSLGPPSMVHYDSQDLDTLFGKSSSPLTESGCPJLSSEE	960
Db	901	SNNLISTIPSDNLAAAGDNTSSLGPPSMVHYDSQDLDTLFGKSSSPLTESGCPJLSSEE	960
Oy	961	NNDKLTLESGLMNSQESMGKNVSSGEGRLFKKRAHGPALLTKNALFKVYSILKTN	1020
Db	961	NNDKLTLESGLMNSQESMGKNVSSGEGRLFKKRAHGPALLTKNALFKVYSILKTN	1020

Oy	1021	KTSNNSATNRKTHIDPSLLIENSPPVNONLIESDEFEKKVPLIHDMRLMDKNAATALRL	1080
Db	1021	KTSNNSATNRKTHIDPSLLIENSPPVNONLIESDEFEKKVPLIHDMRLMDKNAATALRL	1080
Oy	1081	NIMSNTKTTSSKNMEMVOOKKEGPIPPDQANDMSFFMLFLPESARMIORTHGKNSLNSG	1140
Db	1081	NIMSNTKTTSSKNMEMVOOKKEGPIPPDQANDMSFFMLFLPESARMIORTHGKNSLNSG	1140
Oy	1141	OGSPKQVLVSLGPEKSYEGONFLSEKNKVYVKGKEPFDVGLKEMVFPSSRLFLTJNDN	1200
Db	1141	OGSPKQVLVSLGPEKSYEGONFLSEKNKVYVKGKEPFDVGLKEMVFPSSRLFLTJNDN	1200
Oy	1201	LHENTHNOEKKIOEIEKEKTELIOENVLPQIHVGTGNFKMLFLTLSTONVSGSYD	1260
Db	1201	LHENTHNOEKKIOEIEKEKTELIOENVLPQIHVGTGNFKMLFLTLSTONVSGSYD	1260
Oy	1261	GAYAVVLQDFRSLNDSTNRTKKHTAHFSKGBEENLEGJLQNOTKOIVERYACTTRISPT	1320
Db	1261	GAYAVVLQDFRSLNDSTNRTKKHTAHFSKGBEENLEGJLQNOTKOIVERYACTTRISPT	1320
Oy	1321	SOQNFVTOBSKRALQOPRLPLEETELERKIIVDPTSTOMSKNNKHLPTSTLQIDYNEKE	1380
Db	1321	SOQNFVTOBSKRALQOPRLPLEETELERKIIVDPTSTOMSKNNKHLPTSTLQIDYNEKE	1380
Oy	1381	KGATIOSPLSDCLTRSHSIPQANRSPPLAYVSSPISIRIYITRVLFDNSHILPAASY	1440
Db	1381	KGATIOSPLSDCLTRSHSIPQANRSPPLAYVSSPISIRIYITRVLFDNSHILPAASY	1440
Oy	1441	RKSDGVOESSHFLQAGKAKNNLSIALTLTLEMTGDOREVSLGTSATNSVYKKEVNTLP	1500
Db	1441	RKSDGVOESSHFLQAGKAKNNLSIALTLTLEMTGDOREVSLGTSATNSVYKKEVNTLP	1500
Oy	1501	KPDLKPTSGKVELLPKYHIYQXDLPTETSNSGSGHLDLVESLLOGTGCAIKMNEARP	1560
Db	1501	KPDLKPTSGKVELLPKYHIYQXDLPTETSNSGSGHLDLVESLLOGTGCAIKMNEARP	1560
Oy	1561	GVPPFLRATVATSSAKPTSKLDP LANDNHYQTQPKESKMSQKSPKTAFAKKKTITLSL	1620
Db	1561	GVPPFLRATVATSSAKPTSKLDP LANDNHYQTQPKESKMSQKSPKTAFAKKKTITLSL	1620
Oy	1621	NACESNHAIAAININGONKPEIEVYNAKOGRTERLCSQNPVLRKHORPEITRTTLOSQOE	1680
Db	1621	NACESNHAIAAININGONKPEIEVYNAKOGRTERLCSQNPVLRKHORPEITRTTLOSQOE	1680
Oy	1681	EIDYDDTISVEMKKEEDDIYDEBENQSPRSOKTRHYFLAVERIMDYGMSSPHVLRN	1740
Db	1681	EIDYDDTISVEMKKEEDDIYDEBENQSPRSOKTRHYFLAVERIMDYGMSSPHVLRN	1740
Oy	1740	RAQSGSVQPKKVVFOEFTDGSFTQPLIRGELNHLGLGPTIRAEVEDNIMVTFRNDAS	1799
Db	1741	RAQSGSVQPKKVVFOEFTDGSFTQPLIRGELNHLGLGPTIRAEVEDNIMVTFRNDAS	1800
Oy	1800	RPYSFSSLSIYEEBDOQGAEPKKNFVKPNETKTYFNKVOHNAAPTKDEFDCKAAVYFSD	1859
Db	1801	RPYSFSSLSIYEEBDOQGAEPKKNFVKPNETKTYFNKVOHNAAPTKDEFDCKAAVYFSD	1860
Oy	1860	VLEKDVHSGLIGPLVACHNTLNPAGHGOYVQEFALFTTIDETKSWTFENNERKCR	1919
Db	1861	VLEKDVHSGLIGPLVACHNTLNPAGHGOYVQEFALFTTIDETKSWTFENNERKCR	1920
Oy	1920	APCNTOMEDPTFKENYEFNAINGYIMDTLPGLVMAQDRIKMYLLSMGSENIHSHIFSG	1979
Db	1921	APCNTOMEDPTFKENYEFNAINGYIMDTLPGLVMAQDRIKMYLLSMGSENIHSHIFSG	1980
Oy	1980	HVFYVRKKEEKYKMAVLYLVGVEYEMJPMPSAGIMRBECLIGENHJHAQMSLFLVYSNK	2039
Db	1981	HVFYVRKKEEKYKMAVLYLVGVEYEMJPMPSAGIMRBECLIGENHJHAQMSLFLVYSNK	2040
Oy	2040	CQPLGMAHGIHDPQITIASGOYGMAPKPLARLYSSISNAHSTKEPESNIRVVDLAPMI	2099
Db	2041	CQPLGMAHGIHDPQITIASGOYGMAPKPLARLYSSISNAHSTKEPESNIRVVDLAPMI	2100

QY 2100 IHGKIQGAKQKSSLYISQFIIMTSLDGKKWQTYRGNSTGLMWFQSNVSSGIRKNIF 2159  
DB 2101 IHGKIQGAKQKSSLYISQFIIMTSLDGKKWQTYRGNSTGLMWFQSNVSSGIRKNIF 2160  
QY 2160 NPIIARIYIRLHPYHSISIRSLRMEIMCGLDINSCLMPLGKESKATSDAQITASSYFTNM 2219  
DB 2161 NPIIARIYIRLHPYHSISIRSLRMEIMCGLDINSCLMPLGKESKATSDAQITASSYFTNM 2220  
QY 2220 ATWSPSKARLHLOGRSMARPOVNNKREMLQVDFQKTKMYTGVTTQGVKSLTSMYKEF 2279  
DB 2221 ATWSPSKARLHLOGRSMARPOVNNKREMLQVDFQKTKMYTGVTTQGVKSLTSMYKEF 2280  
QY 2280 LISSSDGQHWTLFFONGKVKVQGNODSFTPVVNSLDPRLTLRYLRIRHPOSWVHQIALR 2339  
DB 2281 LISSSDGQHWTLFFONGKVKVQGNODSFTPVVNSLDPRLTLRYLRIRHPOSWVHQIALR 2340  
QY 2340 MEVLGCEADPLY 2351  
DB 2341 MEVLGCEADPLY 2352

RESULT 40  
AAW11451  
ID AAW11451 standard; Protein; 2352 AA.  
AC AAW11451;  
XX 20-NOV-1997 (first entry)  
DE Active Factor VIII:C analogue residue 1647 F/E/P insertion.  
XX  
XX Factor VIII:C: analogue; glycoprotein; blood coagulation cascade;  
KM fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KM plasma protease; thrombin; immunogen; antibody; haemophilia; therapy;  
KM proteolytic cleavage.  
XX  
XX Homo sapiens.  
OS Synthetic.  
FH Key  
FT Peptide 1..19 Location/Qualifiers  
FT /note="signal peptide" 20..2352  
FT Protein  
FT /note="mature Factor VIII:C" 20..1668  
FT Region  
FT /note="heavy chain fragment" 1666  
FT Modified-site /label="Phe, Glu, Pro  
FT /note="inserted residue" 1669..2351  
FT Region  
FT /note="light chain fragment" 760..1668  
FT Domain  
FT /note="B domain"  
XX  
XX W09703195-A1.  
XX  
XX 30-JAN-1997.  
XX  
XX 09-JUL-1996; 96WO-US11444.  
XX  
XX 11-JUL-1995; 95US-0001025.  
XX  
XX (CHIR ) CHIRON CORP.  
XX  
XX Cohen FE, Hung DT, Innis M;  
XX  
XX WPI: 1997-119050/11.  
XX  
XX Factor VIII:C analog modified adjacent to a non-activating Arg  
XX residue - used in the treatment of haemophiliacs, by improvement of  
XX haemostasis  
XX  
XX Claim 34; Page -; 90pp; English.

XX AAW11330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see A0151357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophiliacs, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX  
SQ Sequence 2352 AA:  
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;  
QY 1 MOIELSTCFPLCLLRCSFAPRRYVIGAVELSDMYQMSDLGELPVDARFPPRPKSPFN 60  
DB 1 MOIELSTCFPLCLLRCSFATRRYVIGAVELSDMYQMSDLGELPVDARFPPRPKSPFN 60  
QY 61 TSVYKKTLEVEETHLEINAKRPPMGLLPTDAEYDVTVTLLKNASHPVSLAH 120  
DB 61 TSVYKKTLEVEETHLEINAKRPPMGLLPTDAEYDVTVTLLKNASHPVSLAH 120  
QY 121 GVSYWKASSEGAEYDDOTSOREKEDKVPFGSHTYVYVQYKENGPMASDPLCLTYSLSH 180  
DB 121 GVSYWKASSEGAEYDDOTSOREKEDKVPFGSHTYVYVQYKENGPMASDPLCLTYSLSH 180  
QY 181 VDLVKDLSGLIGALLVREGSLAKKKTQTLHFILFVFPREGSKMSERKNSIMODRD 240  
DB 181 VDLVKDLSGLIGALLVREGSLAKKKTQTLHFILFVFPREGSKMSERKNSIMODRD 240  
QY 241 AASARAMPKMTYNGVYNSRLPGLIGCHRSYVWYVIGCTTPEVHSITFEGHFTVLRNH 300  
DB 241 AASARAMPKMTYNGVYNSRLPGLIGCHRSYVWYVIGCTTPEVHSITFEGHFTVLRNH 300  
QY 301 RQASHLSPTTFLTAOTLMDLGOFLFCHIHSSHODGMEAVVYKDSCEPEPOLRMKNNE 360  
DB 301 RQASHLSPTTFLTAOTLMDLGOFLFCHIHSSHODGMEAVVYKDSCEPEPOLRMKNNE 360  
QY 361 EADYDDDLDSMDVYRPPDDNSPFIQIRYAKKRPRTWYNTAAEERMDVAPLYLA 420  
DB 361 EADYDDDLDSMDVYRPPDDNSPFIQIRYAKKRPRTWYNTAAEERMDVAPLYLA 420  
QY 421 PDDRSYKSYQLNNGPQIRGKKYKVMATYDTFTKRAALQHSGLIGPLLYGEVDTL 480  
DB 421 PDDRSYKSYQLNNGPQIRGKKYKVMATYDTFTKRAALQHSGLIGPLLYGEVDTL 480  
QY 481 LIIFKNQASRPYNTYHGTVDYRPLYSRRLPKGVKRLKQFLLPELPIKRYKMYWYEDDP 540  
DB 481 LIIFKNQASRPYNTYHGTVDYRPLYSRRLPKGVKRLKQFLLPELPIKRYKMYWYEDDP 540  
QY 541 TKSPRCLTRYSSSYNNERDLASGLIGPLLYTKKSVDQRNQJMSKRVYLIFSYFDE 600  
DB 541 TKSPRCLTRYSSSYNNERDLASGLIGPLLYTKKSVDQRNQJMSKRVYLIFSYFDE 600  
QY 601 NRSWYLTENIOTRELPNAGVQLEDEPEQASINHSINGVPEDSLQSVCLHEAVAYWYILS 660  
DB 601 NRSWYLTENIOTRELPNAGVQLEDEPEQASINHSINGVPEDSLQSVCLHEAVAYWYILS 660  
QY 661 IGAQTDLVSFSGITFKHKMYVEDTLTLPPSGEYFVMSKMNQJMLTLCGHNSDRRNNG 720

|||||  
661 IGADPDLVFFSGTTFHKNVYEDTLTLFPSSGETVFKSNENGLMLLCHNSIDFRNG 720  
QY 721 MTALLVSSCDKNTGDYEDSEDISAYLLSKNNAIEPRFSQNSRHPSTROKQFNATTI 780  
Db 721 MTALLVSSCDKNTGDYEDSEDISAYLLSKNNAIEPRFSQNSRHPSTROKQFNATTI 780  
QY 781 PENDIEKTPMFAHRTPMRKIONVSSSDLLMLRQSPTRHGLISLSDQEKAYETFEDDPS 840  
Db 781 PENDIEKTPMFAHRTPMRKIONVSSSDLLMLRQSPTRHGLISLSDQEKAYETFEDDPS 840  
QY 841 PGALDSNNSLSEMTFERPQLRHSQDMYFPESLQRLNKLGTAAATELKIDFVVSST 900  
Db 841 PGALDSNNSLSEMTFERPQLRHSQDMYFPESLQRLNKLGTAAATELKIDFVVSST 900  
QY 901 SNNLISTIPSDMLAAGTONTSSLGPPSMVHYDSOLDPTTLFGKKSSPLTESGGPLSLSE 960  
Db 901 SNNLISTIPSDMLAAGTONTSSLGPPSMVHYDSOLDPTTLFGKKSSPLTESGGPLSLSE 960  
QY 961 NNDKILLESGLMNSQESSMGKNVSTESGRLFGKRAHGPALLTRKDNALFKVYSILKTN 1020  
Db 961 NNDKILLESGLMNSQESSMGKNVSTESGRLFGKRAHGPALLTRKDNALFKVYSILKTN 1020  
QY 1021 KTSNNSATNRKTHITGFSLLIENSPYMONILLESDEKRYTPILHDMMLDMKNATALL 1080  
Db 1021 KTSNNSATNRKTHITGFSLLIENSPYMONILLESDEKRYTPILHDMMLDMKNATALL 1080  
QY 1081 NHMSNKTSSKNMEVQOKKEGPIPPDAONPDMSEFKMLFPRESARMIQRTHGKNSLNSG 1140  
Db 1081 NHMSNKTSSKNMEVQOKKEGPIPPDAONPDMSEFKMLFPRESARMIQRTHGKNSLNSG 1140  
QY 1141 QGSPKQIVSLGPEKSVGONFLSEKNVYVGGETKDVGLKENVPPSSRNLFILNLDN 1200  
Db 1141 QGSPKQIVSLGPEKSVGONFLSEKNVYVGGETKDVGLKENVPPSSRNLFILNLDN 1200  
QY 1201 LHEMNTNNOBKIOEIEIKETLLOENVVLPQTHYTGCKNPKMLLSTRONVGSST 1260  
Db 1201 LHEMNTNNOBKIOEIEIKETLLOENVVLPQTHYTGCKNPKMLLSTRONVGSST 1260  
QY 1261 GAYAPVLODFSLINDSTNRKKAHPSKKKEENLEGLGNQTOIYEKACTTRISPWT 1320  
Db 1261 GAYAPVLODFSLINDSTNRKKAHPSKKKEENLEGLGNQTOIYEKACTTRISPWT 1320  
QY 1321 SQONFYVQSKRALQOFLPLEETELERITIVDTSTOKSMKHLPTSLTQIDYNEKE 1380  
Db 1321 SQONFYVQSKRALQOFLPLEETELERITIVDTSTOKSMKHLPTSLTQIDYNEKE 1380  
QY 1381 KGATOSPISDCLTSHSHSTPOANSRPLPIAKVSSFSSTPIYLRVLFQDNSSHLPAASY 1440  
Db 1381 KGATOSPISDCLTSHSHSTPOANSRPLPIAKVSSFSSTPIYLRVLFQDNSSHLPAASY 1440  
QY 1441 RKDGVQESSHFLQAKKNNLSAILLTLEMTGDOREVSLGTSATNSVTYKKEVENTVL 1500  
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QY 1501 KPDLPTSGVELLPRVHIYQKDLPTETNSGSGHLDLVEGSLLOGEGAIKMNANRP 1560  
Db 1501 KPDLPTSGVELLPRVHIYQKDLPTETNSGSGHLDLVEGSLLOGEGAIKMNANRP 1560  
QY 1561 GKVPFLVPAATESAKPSSLDLPLAMDNHGTQIPEEKKSOEKSPEKTAFAKKDITLSL 1620  
Db 1561 GKVPFLVPAATESAKPSSLDLPLAMDNHGTQIPEEKKSOEKSPEKTAFAKKDITLSL 1620  
QY 1621 NACESNHAIAINEGONKPEIEVTWAKGRTERLCSQNPVLAKRXOREITRTTLOSDE 1680  
Db 1621 NACESNHAIAINEGONKPEIEVTWAKGRTERLCSQNPVLAKRXOREITRTTLOSDE 1680  
QY 1680 EIDYDPTISVEKKKEPDFIDEDENOSRFSOKTRHYIAVEVLMQYKSSPVLN 1739  
Db 1681 EIDYDPTISVEKKKEPDFIDEDENOSRFSOKTRHYIAVEVLMQYKSSPVLN 1740  
QY 1740 RAQSGVPOFKKVVQOEFTDGSFTQPLYRGELNEHGLGPTTAAVEVDNMTFRNQAS 1799  
|||||

Db 1741 RAQSGVPOFKKVVQOEFTDGSFTQPLYRGELNEHGLGPTTAAVEVDNMTFRNQAS 1800  
QY 1800 RPYSEFSSLSIIEEDQROGAEPKRNKYNKNEKTYFKMVQHHAAPTKDEPCKAAYASD 1859  
Db 1801 RPYSEFSSLSIIEEDQROGAEPKRNKYNKNEKTYFKMVQHHAAPTKDEPCKAAYASD 1860  
QY 1860 VDLEKDVHSGILGPLLYCHNTLNPAGHQVQVEFALFETEDETKSWYETENNERCR 1919  
Db 1861 VDLEKDVHSGILGPLLYCHNTLNPAGHQVQVEFALFETEDETKSWYETENNERCR 1920  
QY 1920 APCNIOMEPTFEKRYPRHAINCYINDTLPGIYMAODRIMVYLLMSGNENHSHIFSG 1979  
Db 1921 APCNIOMEPTFEKRYPRHAINCYINDTLPGIYMAODRIMVYLLMSGNENHSHIFSG 1980  
QY 1980 HFTVRRKKEEYKMALYNLPGVEFYEYEMLPKRAGIWREVECLIGESHLAGNSTLFLVYSNK 2039  
Db 1981 HFTVRRKKEEYKMALYNLPGVEFYEYEMLPKRAGIWREVECLIGESHLAGNSTLFLVYSNK 2040  
QY 2040 CQPLMGAGHTRDQITASGOYQONAPKLARLHYSGSINAMSTKEPFSWIKVDLAPMI 2099  
Db 2041 CQPLMGAGHTRDQITASGOYQONAPKLARLHYSGSINAMSTKEPFSWIKVDLAPMI 2100  
QY 2100 IHGKTQGAOKFESSLYSOPITMYSLDGKKQOTYRGSTGTLMVFPFGNDSGIRKHNIF 2159  
Db 2101 IHGKTQGAOKFESSLYSOPITMYSLDGKKQOTYRGSTGTLMVFPFGNDSGIRKHNIF 2160  
QY 2160 NPPIIARYIRLHPHYSTRSTRLNMEIMGCDLNSCMPJGMEKSAISDAQITASSYFTNMF 2219  
Db 2161 NPPIIARYIRLHPHYSTRSTRLNMEIMGCDLNSCMPJGMEKSAISDAQITASSYFTNMF 2220  
QY 2220 ATWSPKARLHLQGSNMAPROVNNPEKMLQYDFOKTKKVTGVTQGVKSLILSMYKBEF 2279  
Db 2221 ATWSPKARLHLQGSNMAPROVNNPEKMLQYDFOKTKKVTGVTQGVKSLILSMYKBEF 2280  
QY 2280 LISSODGHOMTLFQONKQYVPOGNDSTFPVNSLPDLTRVYLRHPOSHVHDIAR 2339  
Db 2281 LISSODGHOMTLFQONKQYVPOGNDSTFPVNSLPDLTRVYLRHPOSHVHDIAR 2340  
QY 2340 MEVLGCEADLY 2351  
Db 2341 MEVLGCEADLY 2352  
  
RESULT 41  
AA011423  
ID AA011423 standard; Protein: 2352 AA.  
XX  
AC AA011423:  
XX  
DT 20-NOV-1997 (first entry)  
XX  
DE Active Factor VIII:C analogue residue 1309 F/E/P insertion.  
XX  
XX Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;  
KM fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KW plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;  
XX proteolytic cleavage.  
XX  
OS Homo sapiens.  
OS Synthetic.  
XX  
FH Key  
FT peptide  
FT  
FT protein  
FT  
FT Region  
FT  
FT  
FT Modified-site  
FT 1328  
FT /label= "Phe, Glu, Pro  
FT /note= "inserted residue"  
FT 1669..2351  
FT  
FT Region  
FT /note= "light chain fragment"

FT Domain 760..1668  
/note= "B domain"  
XX  
PN WO9703195-A1.  
XX 30-JAN-1997.  
XX  
XX 09-JUL-1996; 96WO-US11444.  
XX  
XX 11-JUL-1995; 95US-0001025.  
XX  
XX (CHIR ) CHIRON CORP.  
XX  
XX Cohen FE, Hung DT, Innis M;  
XX WPI; 1997-119050/11.  
XX  
XX Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophiliaacs, by improvement of  
PT haemostasis  
XX  
XX  
PS Claim 28; Page -: 90pp; English.  
XX  
XX AAW11330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAW51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophiliaacs, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX  
SQ Sequence 2352 AA.  
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;  
QY 1 MQELSTCFELCLRFCSATRRYYLGAVELSDYMQSDLGELPYDAFPFPPPKSFPFN 60  
DB 1 MQELSTCFELCLRFCSATRRYYLGAVELSDYMQSDLGELPYDAFPFPPPKSFPFN 60  
QY 61 TSVYVKKTLFVEPTDHLFNIAKPRPPMGLGTTIOAEYDTVYVTLTKNASHVSLAHV 120  
DB 61 TSVYVKKTLFVEPTDHLFNIAKPRPPMGLGTTIOAEYDTVYVTLTKNASHVSLAHV 120  
QY 121 GSVYWKASGAEAYDOTSQREKEDKVPFGSSTYYWQVLKENGPMASDPLCLTLYSLH 180  
DB 121 GSVYWKASGAEAYDOTSQREKEDKVPFGSSTYYWQVLKENGPMASDPLCLTLYSLH 180  
QY 181 VDIYKDLNSGLIGALLVREGSLAKKETOTLHKETLLFPVPEDEKSNHSETKNSLMOODD 240  
DB 181 VDIYKDLNSGLIGALLVREGSLAKKETOTLHKETLLFPVPEDEKSNHSETKNSLMOODD 240  
QY 241 AASARAMPKMTYNGVYVNSLPGLIGCHRSVYWHVIGMTTPEVHSITFEGHTFLVRNH 300  
DB 241 AASARAMPKMTYNGVYVNSLPGLIGCHRSVYWHVIGMTTPEVHSITFEGHTFLVRNH 300  
QY 301 ROASLEISPTFELTAQTLMDLGOFLFCHISSHQHDGMEAVYKDCSPEPOLRKNNNE 360  
DB 301 ROASLEISPTFELTAQTLMDLGOFLFCHISSHQHDGMEAVYKDCSPEPOLRKNNNE 360

QY 361 EADYDDDLTDEMDVYREDDDNPSFIQIRSVAKKHRTVWHYIAAEEEDMDYAPLYA 420  
DB 361 EADYDDDLTDEMDVYREDDDNPSFIQIRSVAKKHRTVWHYIAAEEEDMDYAPLYA 420  
QY 421 PDDRSYKSOYLNNNGPQIRGRKKYKVFREMAVTEDEFEKTEAIOHESGILGPLYGEVDTL 480  
DB 421 PDDRSYKSOYLNNNGPQIRGRKKYKVFREMAVTEDEFEKTEAIOHESGILGPLYGEVDTL 480  
QY 481 LITFKNOASRPYNIYPHGIDVPRPLYSRPLPGVNHLDLPFLIGEFKKMYVYEGDP 540  
DB 481 LITFKNOASRPYNIYPHGIDVPRPLYSRPLPGVNHLDLPFLIGEFKKMYVYEGDP 540  
QY 541 TKSDPRLCTRYYSFVNNERDLASGLIGPLLCYKESVDQGNQIMSDKRNVLISVEDE 600  
DB 541 TKSDPRLCTRYYSFVNNERDLASGLIGPLLCYKESVDQGNQIMSDKRNVLISVEDE 600  
QY 601 NRSWYLTENIOFRLPNPAGVLEDEPEFOASNIHNSINGYVPSIQLSVCLAEVAYVILS 660  
DB 601 NRSWYLTENIOFRLPNPAGVLEDEPEFOASNIHNSINGYVPSIQLSVCLAEVAYVILS 660  
QY 661 IGAOTDFLSVFFSGYTFKKNVYEDTLTLPFSSGFTVMMSMENGCLITLGCNDRRNG 720  
DB 661 IGAOTDFLSVFFSGYTFKKNVYEDTLTLPFSSGFTVMMSMENGCLITLGCNDRRNG 720  
QY 721 MTALLKVVSCDKNTGDIYEDSYEDISAYLLSKNMAIEPRSFSONSRHPSTROKOFNATTI 780  
DB 721 MTALLKVVSCDKNTGDIYEDSYEDISAYLLSKNMAIEPRSFSONSRHPSTROKOFNATTI 780  
QY 781 PENDIKTDPWFARHTPMPKIQONVSSSDILMLROSPTPHGISLSDLOEAKYTFESDPS 840  
DB 781 PENDIKTDPWFARHTPMPKIQONVSSSDILMLROSPTPHGISLSDLOEAKYTFESDPS 840  
QY 841 PGALDSNNSLSMTHTFRQOLHNSDMKTFPESGLQRLNEKLGTAAETELKIDFVVSST 900  
DB 841 PGALDSNNSLSMTHTFRQOLHNSDMKTFPESGLQRLNEKLGTAAETELKIDFVVSST 900  
QY 901 SNNLSTIPSDNLAAGTNTSSLPSPMPVHYDSOLDTTLFGKSSPLTESGGPILSLEE 960  
DB 901 SNNLSTIPSDNLAAGTNTSSLPSPMPVHYDSOLDTTLFGKSSPLTESGGPILSLEE 960  
QY 961 NNSKILSEGLNNSOESSMGKNVSTFSGRLFGRANGPALLTKDNALRKVYSITLKTN 1020  
DB 961 NNSKILSEGLNNSOESSMGKNVSTFSGRLFGRANGPALLTKDNALRKVYSITLKTN 1020  
QY 1021 KTSNNSATNRKTHIDGPELILENSPTWQNIILESDTERKKYTPELIHRMLMDKNATLRL 1080  
DB 1021 KTSNNSATNRKTHIDGPELILENSPTWQNIILESDTERKKYTPELIHRMLMDKNATLRL 1080  
QY 1081 NNSNKTSSKNMEVYQKKEGPIPPDAQNPDKSFFKMLFPESARMIORTHGKNSLNSG 1140  
DB 1081 NNSNKTSSKNMEVYQKKEGPIPPDAQNPDKSFFKMLFPESARMIORTHGKNSLNSG 1140  
QY 1141 QGSPKQOVLSDPEKSVGQNFJSEKKKVVYKGEFTKDVGLAKEVPPSSRNILPLTNLDN 1200  
DB 1141 QGSPKQOVLSDPEKSVGQNFJSEKKKVVYKGEFTKDVGLAKEVPPSSRNILPLTNLDN 1200  
QY 1201 LHEENTHNOEKRIQELIEKKEFTLLIQENVVLPQIHTVYGTKNEMNLFLSTRONVGSST 1260  
DB 1201 LHEENTHNOEKRIQELIEKKEFTLLIQENVVLPQIHTVYGTKNEMNLFLSTRONVGSST 1260  
QY 1261 GAYAPVLOPFRSLNSTRTKTHAHSSKSGEENLEGIQNOTQOIEYKACTTRISPT 1320  
DB 1261 GAYAPVLOPFRSLNSTRTKTHAHSSKSGEENLEGIQNOTQOIEYKACTTRISPT 1320  
QY 1321 SOONFYT-ORSKRALKORLPLEETLEKRIIYDSTQNSKNKKHITPSTLOIDYENK 1379  
DB 1321 SOONFYT-ORSKRALKORLPLEETLEKRIIYDSTQNSKNKKHITPSTLOIDYENK 1379  
QY 1380 EKGATQSPSLDCLTRSHSIPQANRSPPLIAKVSFSPSIRPYLTRVLFODNSHLPAAS 1439  
DB 1380 EKGATQSPSLDCLTRSHSIPQANRSPPLIAKVSFSPSIRPYLTRVLFODNSHLPAAS 1439  
QY 1381 EKGATQSPSLDCLTRSHSIPQANRSPPLIAKVSFSPSIRPYLTRVLFODNSHLPAAS 1440  
DB 1381 EKGATQSPSLDCLTRSHSIPQANRSPPLIAKVSFSPSIRPYLTRVLFODNSHLPAAS 1440



QY	1440	YRKDSGVOESHFLQAGAKNNLSLALTLTLEMTGPOREVGSLGTSATNSVTKKVENTYL	1499
DB	1441	YRKDSGVOESHFLQAGAKNNLSLALTLTLEMTGPOREVGSLGTSATNSVTKKVENTYL	1500
QY	1500	PKPDLPKTSGKVELLPKHVHYQKDLPEPTSSNGSGHLDVGGSLDGTGCAIKMNEANR	1559
DB	1501	PKPDLPKTSGKVELLPKHVHYQKDLPEPTSSNGSGHLDVGGSLDGTGCAIKMNEANR	1560
QY	1560	PGKVPFLRVATESSAKTPSKLLDPLAMDNHYGTQIPKEEMKSQKSEKTAFFKKKDTILS	1619
DB	1561	PGKVPFLRVATESSAKTPSKLLDPLAMDNHYGTQIPKEEMKSQKSEKTAFFKKKDTILS	1620
QY	1620	LNACESNHAIAINNGOKKPEIETVAKGKRTRELCSONPYLKRHOEITRTTLOSDE	1679
DB	1621	LNACESNHAIAINNGOKKPEIETVAKGKRTRELCSONPYLKRHOEITRTTLOSDE	1680
QY	1680	EIDYDITISVEKKKEDFDIYDEENOSPSPFOKTRHFFIAVERLMDYGMSSSPHYLRN	1739
DB	1681	EIDYDITISVEKKKEDFDIYDEENOSPSPFOKTRHFFIAVERLMDYGMSSSPHYLRN	1740
QY	1740	RAQSGSVPOFKKRVPOEFTDGSFTOPLYRGELNHLGLGPIYIRAEVEDNIMVTFENQAS	1799
DB	1741	RAQSGSVPOFKKRVPOEFTDGSFTOPLYRGELNHLGLGPIYIRAEVEDNIMVTFENQAS	1800
QY	1800	RPYSFYSLSIYEEOGAGEPKRNFKYKNETKTYFMWVOHMAPTREDFDCKAMAYFSD	1859
DB	1801	RPYSFYSLSIYEEOGAGEPKRNFKYKNETKTYFMWVOHMAPTREDFDCKAMAYFSD	1860
QY	1860	VDLEKDVHSGLIGPLLVCHNTLMPAHGROVTVQERAPLFTIEDETKSWYFTENMERNCR	1919
DB	1861	VDLEKDVHSGLIGPLLVCHNTLMPAHGROVTVQERAPLFTIEDETKSWYFTENMERNCR	1920
QY	1920	APCNIQMEDPTKEKYNRHAINGYIMDTLPGLVMAODRIMWYLLSGMSNENHSHIFSG	1979
DB	1921	APCNIQMEDPTKEKYNRHAINGYIMDTLPGLVMAODRIMWYLLSGMSNENHSHIFSG	1980
QY	1980	HVFTVARKKEEYKMAIYNYPGVETVEYMLPSKAGIMRVECLIGSHIAKSGSTFLVYSNK	2039
DB	1981	HVFTVARKKEEYKMAIYNYPGVETVEYMLPSKAGIMRVECLIGSHIAKSGSTFLVYSNK	2040
QY	2040	CQTPPLGMAAGHIRDFOITASGOYQNAFKLARLHSGSINAMSTKEPFSWIKVDLLAPMI	2099
DB	2041	CQTPPLGMAAGHIRDFOITASGOYQNAFKLARLHSGSINAMSTKEPFSWIKVDLLAPMI	2100
QY	2100	IHGKITOGAROKFSSLYISOFIIMYSLDGKKMQYTRGNSGTGLMVFNGVNDSSGIGHNIF	2159
DB	2101	IHGKITOGAROKFSSLYISOFIIMYSLDGKKMQYTRGNSGTGLMVFNGVNDSSGIGHNIF	2160
QY	2160	NPPIIARIYRLHPHYSTRFLRMEIEMGCDLNSCSPILGMSKAIISDAQTASSYFTNMF	2219
DB	2161	NPPIIARIYRLHPHYSTRFLRMEIEMGCDLNSCSPILGMSKAIISDAQTASSYFTNMF	2220
QY	2220	ATWSPSKARLHLQGRSNMARPQVNNKREMLQVDFOKTKMVTGVTTQGVKSLTSMYKEEF	2279
DB	2221	ATWSPSKARLHLQGRSNMARPQVNNKREMLQVDFOKTKMVTGVTTQGVKSLTSMYKEEF	2280
QY	2280	LISSSODGHQWTLFPQNGKVKVFOGNDSTFPVYNSLDPPLLTRYLRIHQSVWVHJALR	2339
DB	2281	LISSSODGHQWTLFPQNGKVKVFOGNDSTFPVYNSLDPPLLTRYLRIHQSVWVHJALR	2340
QY	2340	MEVLGCEAODLY 2351	
DB	2341	MEVLGCEAODLY 2352	

DE	Active Factor VIII:C analogue residue 1313 P insertion.
KW	Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW	fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW	plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;
KW	proteolytic cleavage.
OS	Homo sapiens.
OS	Synthetic.
FH	Key
FT	Peptide
FT	Location/Qualifiers
FT	1..19
FT	/note="signal peptide"
FT	20..2352
FT	/note="mature Factor VIII:C"
FT	20..1668
FT	/note="heavy chain fragment"
FT	Misc-difference 1332
FT	/note="inserted residue"
FT	1669..2351
FT	/note="light chain fragment"
FT	760..1668
FT	/note="B domain"
XX	
PN	MO9703195-A1.
XX	
PD	30-JAN-1997.
XX	
PF	09-JUL-1996; 96MO-US11444.
XX	
PR	11-JUL-1995; 95US-0001025.
XX	
PA	(CHIR ) CHIRON CORP.
XX	
PI	Cohen FE, Hung DT, Innis M;
XX	
DR	WPI: 1997-119050/11.
XX	
PT	Factor VIII:C analog modified adjacent to a non-activating Arg
PT	residue - used in the treatment of haemophilias, by improvement of
PT	haemostasis
XX	
XX	Claim 29: Page -: 90pp; English.
XX	
CC	AAW11330-W11472 represent active Factor VIII:C analogues of the
CC	invention. These sequences were created by mutating the wild type Factor
CC	VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC	analogues comprise a native Factor VIII:C polypeptide modified at a site
CC	adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC	dipeptide is created. Factor VIII:C is a large glycoprotein that
CC	participates in the blood coagulation cascade that ultimately converts
CC	soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC	deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC	X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC	activated by plasma proteases, such as thrombin. During activation the
CC	mature polypeptide is cleaved to generate heavy and light chain fragments
CC	that are further cleaved. Complexes of two or more of the analogues,
CC	nucleic acids and vectors encoding them may be used alone or in
CC	conjunction with each other, for the prevention or treatment of active
CC	Factor VIII:C deficiency in a mammal. The analogues may be used as
CC	immunogens to raise antibodies, and in the treatment of haemophilias, by
CC	improvement of haemostasis. The analogues are resistant to proteolytic
CC	cleavage and display increased plasma half-life. They may be administered
CC	at lower dosages and by different modes of administration.
XX	
XX	Sequence 2352 AA:
QY	Query Match 99.9%; Score 12407.5; DB 18; Length 2352;
XX	Best Local Similarity 100.0%; Pred. No. 0;
XX	Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;
XX	1 MOTELNCFELCLAFCSATRRYYLGAVALSDMWQSDIGETLVDAFPFRPKSFPN 60
XX	

Db 1 M01ELSTCFELCLLRFCSATRRYYIGAVELSMWQSDGLBEPVDA RPPRPVKSEPPN 60  
QY 61 TSVYKRTLEVEFTDHLFNIAKPRPMMGLGPTIOAEYDTVVITLKNMASHPVSLAAV 120  
Db 62 TSVYKRTLEVEFTDHLFNIAKPRPMMGLGPTIOAEYDTVVITLKNMASHPVSLAAV 120  
QY 121 GSVYKASGAEYDQTSOREKEDKVFPGSGSHYVQVILKENGPMASDCLCTYSYSH 180  
Db 121 GSVYKASGAEYDQTSOREKEDKVFPGSGSHYVQVILKENGPMASDCLCTYSYSH 180  
QY 181 VDLVQOLNSGLIGALLVCBEGSLAKEKTQTLAKFILLFAVDECKSWHSETKNSLMQDD 240  
Db 181 VDLVQOLNSGLIGALLVCBEGSLAKEKTQTLAKFILLFAVDECKSWHSETKNSLMQDD 240  
QY 241 AASARAMPKMHVNGVNRSLPLGICGHRKSVWHVIGMGTTPVHSLFEGHTEFLVRNH 300  
Db 241 AASARAMPKMHVNGVNRSLPLGICGHRKSVWHVIGMGTTPVHSLFEGHTEFLVRNH 300  
QY 301 ROSLEISPLTFLAQTLDLMDLGOFLFCHISSHQDHGMEAVVADSCPEEPOLRKKNH 360  
Db 301 ROSLEISPLTFLAQTLDLMDLGOFLFCHISSHQDHGMEAVVADSCPEEPOLRKKNH 360  
QY 361 EADYDDDLTJSEMDYVRFDDNSPSFIQIRSVAKKHRTVWHVIAAEEDMDYAPLVLA 420  
Db 361 EADYDDDLTJSEMDYVRFDDNSPSFIQIRSVAKKHRTVWHVIAAEEDMDYAPLVLA 420  
QY 421 PDDRSYKSOYLNNGPORIGRKYKKVRFMAYPDTEFKTREALIOHSGSLIGLGLGEVDTL 480  
Db 421 PDDRSYKSOYLNNGPORIGRKYKKVRFMAYPDTEFKTREALIOHSGSLIGLGLGEVDTL 480  
QY 481 LITFKQASRPYNTIPIHGITDVRPLYSRRLPKGVKHLKDFLLGELFKKKTWYVEDGP 540  
Db 481 LITFKQASRPYNTIPIHGITDVRPLYSRRLPKGVKHLKDFLLGELFKKKTWYVEDGP 540  
QY 541 TKSDPRLCTRRYSSPVNMRDLASGLIGPLLCYKESVDQKNOJMSDKRNVLLFSEVDE 600  
Db 541 TKSDPRLCTRRYSSPVNMRDLASGLIGPLLCYKESVDQKNOJMSDKRNVLLFSEVDE 600  
QY 601 NRSWYLTENIOFELPNPAGVQLEDEPFQASNIHMSINGVYVDSIQLSVCHEVAAYTILS 660  
Db 601 NRSWYLTENIOFELPNPAGVQLEDEPFQASNIHMSINGVYVDSIQLSVCHEVAAYTILS 660  
QY 661 IGAQDPLSVFPGSGTFFKHKWYEDITLTPFPGSETFMSKBNPGLMILCCHNSDFRNG 720  
Db 661 IGAQDPLSVFPGSGTFFKHKWYEDITLTPFPGSETFMSKBNPGLMILCCHNSDFRNG 720  
QY 721 MTALLAVSSCDKNTGDYEDSYEDISAYLLSKNNAIEPRSFQNSRHPSTROKOFNATTI 780  
Db 721 MTALLAVSSCDKNTGDYEDSYEDISAYLLSKNNAIEPRSFQNSRHPSTROKOFNATTI 780  
QY 781 PENDIKETDPMFAHNTPMRKIONVSSDDLMLROSPTPHGLSLSDLOEAKYTFESDDPS 840  
Db 781 PENDIKETDPMFAHNTPMRKIONVSSDDLMLROSPTPHGLSLSDLOEAKYTFESDDPS 840  
QY 841 PGALDSNNLSLMTFRPOLHSGDWYTFPESGLQRLNEKLGTTAATELKIDFVVSST 900  
Db 841 PGALDSNNLSLMTFRPOLHSGDWYTFPESGLQRLNEKLGTTAATELKIDFVVSST 900  
QY 901 SNNLITIPSDMLAGTDMNTSSLPPSPMPVHYDSQLDLTTLGKKSPLTLESGLSLSE 960  
Db 901 SNNLITIPSDMLAGTDMNTSSLPPSPMPVHYDSQLDLTTLGKKSPLTLESGLSLSE 960  
QY 961 NNDKILLESGLMNSOESSGKNVSTSESGRLKGRANGPMLLKDNALKKVYSILTKN 1020  
Db 961 NNDKILLESGLMNSOESSGKNVSTSESGRLKGRANGPMLLKDNALKKVYSILTKN 1020  
QY 1021 KTSNNSATNRKTHIDGPSLILENSPLYWONILLESDETERKATPLIHDRLMDKNATATL 1080  
Db 1021 KTSNNSATNRKTHIDGPSLILENSPLYWONILLESDETERKATPLIHDRLMDKNATATL 1080  
QY 1081 NMSNKTTSKKNMEVQOKKRGPIPPDAONPDMSPFFKMLFPEASARMIORTHKNKNSLNG 1140  
Db 1081 NMSNKTTSKKNMEVQOKKRGPIPPDAONPDMSPFFKMLFPEASARMIORTHKNKNSLNG 1140

QY 1141 QGSPKQVLSLQPEKSVGONFLSEKNKYVVGKGEFTKDVGLKEMFPPSSRNLFLTLNDN 1200  
Db 1141 QGSPKQVLSLQPEKSVGONFLSEKNKYVVGKGEFTKDVGLKEMFPPSSRNLFLTLNDN 1200  
QY 1201 LHNENTHNOEKKIOEIEIKKETLIOENVVLPQIHTVGTGKFKFNKLFLLSTRONVGSYD 1260  
Db 1201 LHNENTHNOEKKIOEIEIKKETLIOENVVLPQIHTVGTGKFKFNKLFLLSTRONVGSYD 1260  
QY 1261 GAYAPVLODFRSLNDSTNRKTHAPSKKGEENLBEGLQTKOYIEXACTTRISPT 1320  
Db 1261 GAYAPVLODFRSLNDSTNRKTHAPSKKGEENLBEGLQTKOYIEXACTTRISPT 1320  
QY 1321 SQONFVYQKSK - FALKQFRPLSETELEKRIIVDDTSTQWSKNKHLTPSTLOIDYNEK 1379  
Db 1321 SQONFVYQKSK - FALKQFRPLSETELEKRIIVDDTSTQWSKNKHLTPSTLOIDYNEK 1379  
QY 1380 EKGATQSPSLDCLTRSHSTPOANRSPPLFIAVSSPSPRIYTLRYLRQDANSHLPAAS 1439  
Db 1380 EKGATQSPSLDCLTRSHSTPOANRSPPLFIAVSSPSPRIYTLRYLRQDANSHLPAAS 1439  
QY 1440 YRKKDSGVQESSHFLQKAKKNLSLAILTEMTGDQREVSGJTSATNSVYKYVENTVL 1499  
Db 1440 YRKKDSGVQESSHFLQKAKKNLSLAILTEMTGDQREVSGJTSATNSVYKYVENTVL 1499  
QY 1500 PKPDLPKTSGVLELLPKVHIYOKDLPPTETSGSPGHLDLVSGSLQGTGGAIKWNEANR 1559  
Db 1500 PKPDLPKTSGVLELLPKVHIYOKDLPPTETSGSPGHLDLVSGSLQGTGGAIKWNEANR 1559  
QY 1560 PKGVPLRYATSSSKPTSKLPLPAMDHYGTCQIPKEBKSQKSEPKARKKDTILS 1619  
Db 1560 PKGVPLRYATSSSKPTSKLPLPAMDHYGTCQIPKEBKSQKSEPKARKKDTILS 1619  
QY 1620 LMACESNHAIAINEGONKPEIEVYAKQRTERLCSQNPVYLKRRQREITRTQLQSDQ 1679  
Db 1620 LMACESNHAIAINEGONKPEIEVYAKQRTERLCSQNPVYLKRRQREITRTQLQSDQ 1679  
QY 1680 EIDYDPTISVEKKKDDPIYDEDENOSPSFQKTRHYFAAVRRLMDGMSSPHYLRN 1739  
Db 1680 EIDYDPTISVEKKKDDPIYDEDENOSPSFQKTRHYFAAVRRLMDGMSSPHYLRN 1739  
QY 1740 RAOSGSVPQFKKVFQFETDGSFTQPLRYGELNEHLGLGFRYIAAEVDINMYTRNOAS 1799  
Db 1740 RAOSGSVPQFKKVFQFETDGSFTQPLRYGELNEHLGLGFRYIAAEVDINMYTRNOAS 1799  
QY 1800 RPYSFYSSLSIYEEDORGAEPKKNFVKPNETKTYFMVQHHAAPTKDEDFCKAMAYFSD 1859  
Db 1800 RPYSFYSSLSIYEEDORGAEPKKNFVKPNETKTYFMVQHHAAPTKDEDFCKAMAYFSD 1859  
QY 1860 VDEKDVHSGLIGPLVCHNTLNPAGROVYVOEFALFPTIFPETKSWYTFENNERCR 1919  
Db 1860 VDEKDVHSGLIGPLVCHNTLNPAGROVYVOEFALFPTIFPETKSWYTFENNERCR 1919  
QY 1920 APCNIDMEPPTKERYRHAINGYIMDTLPGLVMAQDORIMWYLLSGSNENHSHHSFG 1979  
Db 1920 APCNIDMEPPTKERYRHAINGYIMDTLPGLVMAQDORIMWYLLSGSNENHSHHSFG 1979  
QY 1980 HFTYVRKKEEYKMAIYNLYPGEVEYEMLPKRAKIMRVECLIGEHLLAGNSTLFLVSNK 2039  
Db 1980 HFTYVRKKEEYKMAIYNLYPGEVEYEMLPKRAKIMRVECLIGEHLLAGNSTLFLVSNK 2039  
QY 2040 COTPLGMAHGHROFOITASGOYGOAARPLATLHSGSINAKSKKEPFSIKYVDLAPMI 2099  
Db 2040 COTPLGMAHGHROFOITASGOYGOAARPLATLHSGSINAKSKKEPFSIKYVDLAPMI 2099  
QY 2100 COTPLGMAHGHROFOITASGOYGOAARPLATLHSGSINAKSKKEPFSIKYVDLAPMI 2100  
Db 2100 COTPLGMAHGHROFOITASGOYGOAARPLATLHSGSINAKSKKEPFSIKYVDLAPMI 2100  
QY 2160 NPTIARVRLAPTHYSIRSTLRKLELMGCDLWCSGMPGMSKRAISDAQITLASSYFTNMF 2219  
Db 2160 NPTIARVRLAPTHYSIRSTLRKLELMGCDLWCSGMPGMSKRAISDAQITLASSYFTNMF 2219

QY 2220 ATWSPSKARLHLOGSNMARPQVNNREKLVDFQRTKKTGVTGCVSKLTSMTYKEF 2279  
DB 2221 ATWSPSKARLHLOGSNMARPQVNNREKLVDFQRTKKTGVTGCVSKLTSMTYKEF 2280  
QY 2280 LISSSDGQHQMFLFPGNGKVKVFEQGNDSFTFVNSLDPPLLTFRYLRIHPQSVWQIALR 2339  
DB 2281 LISSSDGQHQMFLFPGNGKVKVFEQGNDSFTFVNSLDPPLLTFRYLRIHPQSVWQIALR 2340  
QY 2340 MEVLGCEADPLY 2351  
DB 2341 MEVLGCEADPLY 2352

RESULT 43  
AAW11429 standard; Protein: 2352 AA.  
AAW11429;  
20-NOV-1997 (first entry)  
Active Factor VIII:C analogue residue 1314 P insertion.  
Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;  
fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;  
proteolytic cleavage.  
Homo sapiens.  
Synthetic.  
Key Location/Qualifiers  
FH 1..19  
FT /note= "Signal peptide"  
FT Protein 20..2352  
FT /note= "mature Factor VIII:C"  
FT Region 20..1668  
FT /note= "heavy chain fragment"  
FT Misc-difference 1335  
FT /note= "inserted residue"  
FT Region 1669..2351  
FT /note= "light chain fragment"  
FT Domain 760..1668  
FT /note= "B domain"  
MO9703195-A1.  
30-JAN-1997.  
09-JUL-1996; 96MO-US11444.  
11-JUL-1995; 9505-0001025.  
(CHIR ) CHIRON CORP.  
Cohen FE, Hung DT, Innis M;  
WPI: 1997-119050/11.  
Factor VIII:C analog modified adjacent to a non-activating Arg  
residue, used in the treatment of haemophiliacs, by improvement of  
haemostasis  
Claim 29; Page -: 90pp; English.  
AAW11330-W11472 represent active Factor VIII:C analogues of the  
invention. These sequences were created by mutating the wild type Factor  
VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
analogues comprise a native Factor VIII:C polypeptide modified at a site  
adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
dipeptide is created. Factor VIII:C is a large glycoprotein that  
participates in the blood coagulation cascade that ultimately converts  
soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A

CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophiliacs, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
SQ Sequence 2352 AA:  
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;  
QY 1 M0IELSTCFPLCLARFCPSATRRYYLGAVELSMQWQSDGLPVDARPPVPKSPFFN 60  
DB 1 M0IELSTCFPLCLARFCPSATRRYYLGAVELSMQWQSDGLPVDARPPVPKSPFFN 60  
QY 61 TSVYVKKTLFVETDHLPLNTAKRPPMGLLPTQAEVYDVTYTLKNASHPVSLAY 120  
DB 61 TSVYVKKTLFVETDHLPLNTAKRPPMGLLPTQAEVYDVTYTLKNASHPVSLAY 120  
QY 121 GVSVMKASGAEYDQTSQREKEDDKVPFGSGHTVYMWOLKENGPMASDPLCLTYSLSH 180  
DB 121 GVSVMKASGAEYDQTSQREKEDDKVPFGSGHTVYMWOLKENGPMASDPLCLTYSLSH 180  
QY 181 VDLVKDLSGLIGALLVCREGSLAKEKQTLKHFLLFAVDEGSKSHSEFTNSLMQDRD 240  
DB 181 VDLVKDLSGLIGALLVCREGSLAKEKQTLKHFLLFAVDEGSKSHSEFTNSLMQDRD 240  
QY 241 AASARAPKMHVNVNGYVRSILPGLICGHRKSYVMYVIMGTPEVHSIFLEGTFELVNH 300  
DB 241 AASARAPKMHVNVNGYVRSILPGLICGHRKSYVMYVIMGTPEVHSIFLEGTFELVNH 300  
QY 241 AASARAPKMHVNVNGYVRSILPGLICGHRKSYVMYVIMGTPEVHSIFLEGTFELVNH 300  
DB 241 AASARAPKMHVNVNGYVRSILPGLICGHRKSYVMYVIMGTPEVHSIFLEGTFELVNH 300  
QY 301 ROASLSITPTFLNQTLLMDLQGLFLFCHISHOHDMKEMAYVNDSCPEEQLRKKNNE 360  
DB 301 ROASLSITPTFLNQTLLMDLQGLFLFCHISHOHDMKEMAYVNDSCPEEQLRKKNNE 360  
QY 361 EAEYDDDLTDEMDVNFDDNSPSFIOIRSAVKKHPRTVWHYIAAEEDMDYAPLVLA 420  
DB 361 EAEYDDDLTDEMDVNFDDNSPSFIOIRSAVKKHPRTVWHYIAAEEDMDYAPLVLA 420  
QY 421 PDDRSYKSOYLNGPQRIGRKYYKVRPMAYTETPTREAIQHSGLIGPLLYGEGDTL 480  
DB 421 PDDRSYKSOYLNGPQRIGRKYYKVRPMAYTETPTREAIQHSGLIGPLLYGEGDTL 480  
QY 481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPGVXHLKDFPLDELFKTKWTVEEDGP 540  
DB 481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPGVXHLKDFPLDELFKTKWTVEEDGP 540  
QY 541 TKSDPRCLFRYYSSFVNNERDLASGLGPLLICYESVDQGNQIMSDKRNVLFSFDE 600  
DB 541 TKSDPRCLFRYYSSFVNNERDLASGLGPLLICYESVDQGNQIMSDKRNVLFSFDE 600  
QY 601 NRSWYLTENIOERLPNAGVLEDEPEQASNIHSGINCYVDSIQLSVCHAEAVYITLS 660  
DB 601 NRSWYLTENIOERLPNAGVLEDEPEQASNIHSGINCYVDSIQLSVCHAEAVYITLS 660  
QY 661 IGAOTDFLSVFFSGYTFKHKVYEDTLTLPFSGEYFMSMENGLMILICHNSDFRNG 720  
DB 661 IGAOTDFLSVFFSGYTFKHKVYEDTLTLPFSGEYFMSMENGLMILICHNSDFRNG 720  
QY 721 MTVALKVSCKDNQDYEDYEDISAYLTKNNMIEPRSPQNSRHPSTROKOFNATTI 780  
DB 721 MTVALKVSCKDNQDYEDYEDISAYLTKNNMIEPRSPQNSRHPSTROKOFNATTI 780  
QY 781 PENDIKTPWFAHTTBMPTKIQONVSSDILMLRQSPHLSLSDQEKKYTESDPS 840  
DB 781 PENDIKTPWFAHTTBMPTKIQONVSSDILMLRQSPHLSLSDQEKKYTESDPS 840

Db 781 PENDIEKTDPMFAHRTPMKIQNVSSDLMLROSPTPHGLSLSDLOEAKYETFDSDPS 840  
QY 841 PGAIIDSNNSLSBMTJFHPOLHHSQDMWFTPEGLOLRNLEKLTGTTAATELKRIDFVVSST 900  
Db 841 PGAIIDSNNSLSBMTJFHPOLHHSQDMWFTPEGLOLRNLEKLTGTTAATELKRIDFVVSST 900  
QY 901 SNNLISTIPSDMLAGCTNNTSSLCGPPSMYPHDSOLDLTTLGKSSPLTSSGSPLSISE 960  
Db 901 SNNLISTIPSDMLAGCTNNTSSLCGPPSMYPHDSOLDLTTLGKSSPLTSSGSPLSISE 960  
QY 961 NDSKILLESGLMNSQESSWGKNVSTESGRLEKGRARAGPALLTKRDNALEKVSISLTKTN 1020  
Db 961 NDSKILLESGLMNSQESSWGKNVSTESGRLEKGRARAGPALLTKRDNALEKVSISLTKTN 1020  
QY 1021 KTSNNSATNRKTHIDGPFLLIENSFWONITLESPTDEFEKKTPLIHRMIMDKNATLRL 1080  
Db 1021 KTSNNSATNRKTHIDGPFLLIENSFWONITLESPTDEFEKKTPLIHRMIMDKNATLRL 1080  
QY 1081 NMSNKTTSKKMEVQOKKEGPTPPDAQNPDMSPFKMLFPESAKMTQRTGKNSLNG 1140  
Db 1081 NMSNKTTSKKMEVQOKKEGPTPPDAQNPDMSPFKMLFPESAKMTQRTGKNSLNG 1140  
QY 1141 QGSPKQOLVSLGPEKSVGQNFLEKKNVVGKEFTKDVGLKEMVPPSSRNLFETNLDN 1200  
Db 1141 QGSPKQOLVSLGPEKSVGQNFLEKKNVVGKEFTKDVGLKEMVPPSSRNLFETNLDN 1200  
QY 1201 LHEHNTNHOEKKIOEIEKKEFTLIOENVVLPOIHTVTGKKNFMKLFLLSTRONVGSYD 1260  
Db 1201 LHEHNTNHOEKKIOEIEKKEFTLIOENVVLPOIHTVTGKKNFMKLFLLSTRONVGSYD 1260  
QY 1261 GAYAPVLODPBSLINTSTRTKTHAHFSKGEENLEGINOTQOIEYKACTRTISPT 1320  
Db 1261 GAYAPVLODPBSLINTSTRTKTHAHFSKGEENLEGINOTQOIEYKACTRTISPT 1320  
QY 1321 SQONFVTOBSKR-ALKOFRPLBEETLEKRIIVDDTSTOWSKNKHLPSTLQIDYNEK 1379  
Db 1321 SQONFVTOBSKR-ALKOFRPLBEETLEKRIIVDDTSTOWSKNKHLPSTLQIDYNEK 1380  
QY 1380 EKGATQSPPLSDCLTRSHSIPQANRSPPLIAKVSPPSIRPLIYLRVLPQDONSHPAAS 1439  
Db 1381 EKGATQSPPLSDCLTRSHSIPQANRSPPLIAKVSPPSIRPLIYLRVLPQDONSHPAAS 1440  
QY 1440 YRKKDSGVOESSHFLQGAKKNNLSLALITLDMTGQOREVSGLSGTSAINSTYTKKVENTVL 1499  
Db 1441 YRKKDSGVOESSHFLQGAKKNNLSLALITLDMTGQOREVSGLSGTSAINSTYTKKVENTVL 1500  
QY 1500 PKPDLPRKTSQKVELLPKVHIYQKDLFPTETSNQSPGHLDLVEGSLQGTGAIKMEANR 1559  
Db 1501 PKPDLPRKTSQKVELLPKVHIYQKDLFPTETSNQSPGHLDLVEGSLQGTGAIKMEANR 1560  
QY 1560 PGKVPFLRATETSSAKTSPSKLLDPLANDNHYGQIPKEEMKSOEKSPKTAFFKKDTIIS 1619  
Db 1561 PGKVPFLRATETSSAKTSPSKLLDPLANDNHYGQIPKEEMKSOEKSPKTAFFKKDTIIS 1620  
QY 1620 LNCESNHAIAAINEGOKNPEIETWAKOGRTRLCSQNPYLRKHOREITRTTLOSDE 1679  
Db 1621 LNCESNHAIAAINEGOKNPEIETWAKOGRTRLCSQNPYLRKHOREITRTTLOSDE 1680  
QY 1680 EIDYDDTISVEMKKEDFIYDEDENOSPFSOKTTHYETIAAVERLMDYGMSSPVLN 1739  
Db 1681 EIDYDDTISVEMKKEDFIYDEDENOSPFSOKTTHYETIAAVERLMDYGMSSPVLN 1740  
QY 1740 RAQGSVPQKVVYFOETDGSFTQPLRGELNENHGLIPYIRAEVDNIMTFNQS 1799  
Db 1741 RAQGSVPQKVVYFOETDGSFTQPLRGELNENHGLIPYIRAEVDNIMTFNQS 1800  
QY 1800 RPYSTFSSLSISTEBDOGGAEPKKNVYKPNETKTYTWKVOHMAPTOEDFCAMAYFSD 1859  
Db 1801 RPYSTFSSLSISTEBDOGGAEPKKNVYKPNETKTYTWKVOHMAPTOEDFCAMAYFSD 1860  
QY 1860 VDLEKDVHSLGLGPLVLCNTLNPAGROVYTOEALFETTFDETKSWYFTEMERNCR 1919  
Db 1861 VDLEKDVHSLGLGPLVLCNTLNPAGROVYTOEALFETTFDETKSWYFTEMERNCR 1920

QY 1920 APCNIQMEDPTREKENTRPHALINGYINDTLPGLVMAQDORIRWYLLSGKSNENIHSIESG 1979  
Db 1921 APCNIQMEDPTREKENTRPHALINGYINDTLPGLVMAQDORIRWYLLSGKSNENIHSIESG 1980  
QY 1980 HVTYVRKREYEMALYNLYGVEFETVEMLPKRAGIWRECELGEBHLHAGMSTFLYVSNK 2039  
Db 1981 HVTYVRKREYEMALYNLYGVEFETVEMLPKRAGIWRECELGEBHLHAGMSTFLYVSNK 2040  
QY 2040 CQTPUGMASGHTROFQTASGQIGQAPKLAHLHSSGINASTKEPFSIKYDILAPMI 2099  
Db 2041 CQTPUGMASGHTROFQTASGQIGQAPKLAHLHSSGINASTKEPFSIKYDILAPMI 2100  
QY 2100 IHGIKTQAGARKFSSLSYISQFIIMYSLSDEKKNQOTYRGNSGTGLWVFGVNDSSGLKHNIF 2159  
Db 2101 IHGIKTQAGARKFSSLSYISQFIIMYSLSDEKKNQOTYRGNSGTGLWVFGVNDSSGLKHNIF 2160  
QY 2160 NPPLIARVLRHPTHYSTRSLRHELMGCDLNSGSMPLGMSKASISDAQTASVFTNMF 2219  
Db 2161 NPPLIARVLRHPTHYSTRSLRHELMGCDLNSGSMPLGMSKASISDAQTASVFTNMF 2220  
QY 2220 ATWSPSKARLHLOGSNAMRPQVNNREKMLQVDFOKTYKVTGVTQGVKSLTSMYKEF 2279  
Db 2221 ATWSPSKARLHLOGSNAMRPQVNNREKMLQVDFOKTYKVTGVTQGVKSLTSMYKEF 2280  
QY 2280 LISSODGHQMTLFPONGKVKVFPQGNDSFTPVNSLDPPLTFYRLRIHPQSVMHQIALR 2339  
Db 2281 LISSODGHQMTLFPONGKVKVFPQGNDSFTPVNSLDPPLTFYRLRIHPQSVMHQIALR 2340  
QY 2340 MEYVIGCEADQDY 2351  
Db 2341 MEYVIGCEADQDY 2352

RESULT 44  
AAW11433  
ID AAW11433 standard; Protein: 2352 AA.  
XX  
AC AAW11433;  
XX  
DT 20-NOV-1997 (first entry)  
XX  
DE Active Factor VIII:C analogue residue 1312 F/E/P insertion.  
XX  
KW Factor VIII:C; analogue: glycoprotein; blood coagulation cascade;  
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KW plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;  
XX proteolytic cleavage.  
OS  
OS Homo sapiens.  
OS Synthetic.  
XX  
FH Key Location/Qualifiers  
FT Peptide 1..19  
FT Protein 20..2352  
FT Region /note= "mature Factor VIII:C"  
FT Region 20..1668  
FT Modified-site /note= "heavy chain fragment"  
FT 1331  
FT /label= "Phe, Glu, Pro  
FT /note= "inserted residue"  
FT 1669..2351  
FT /note= "light chain fragment"  
FT 760..1668  
FT Domain /note= "B domain"  
XX  
XX W09703195-A1.  
XX PN  
XX 30-JAN-1997.  
XX PD  
XX 09-JUL-1996; 96WC-US11444.  
XX

PR 11-JUL-1995; 9505-0001025.  
PA (CHIR ) CHIRON CORP.  
XX  
PI Cohen FE, Hung DT, Innis M;  
XX WPI; 1997-119050/11.  
XX  
PT Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophilias, by improvement of  
PT haemostasis  
XX  
XX  
PS Claim 30: Page -: 90pp: English.  
XX  
XX AAM11330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophilias, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX  
XX  
SO Sequence 2352 AA:  
  
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;  
Best Local Similarity 100.0%; Pred. NO. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

QY 481 LIFKNOASPPNITPHGIDTVRPVLSRLPGVGHKLDQFILLGCEIFKTKWTYVEDP 540  
DB 481 LIFKNOASPPNITPHGIDTVRPVLSRLPGVGHKLDQFILLGCEIFKTKWTYVEDP 540  
QY 541 TKSDPCLRTYRYSFVNMNERDLASGLIGPLLCYKESYDQGNQIMSDKRNVTLEFVEDE 600  
DB 541 TKSDPCLRTYRYSFVNMNERDLASGLIGPLLCYKESYDQGNQIMSDKRNVTLEFVEDE 600  
QY 601 NRSWYLTENTORFLNPNAGVOLDEPPEQASNTMHSINQVSDQLSVCHAYAVYITLS 660  
DB 601 NRSWYLTENTORFLNPNAGVOLDEPPEQASNTMHSINQVSDQLSVCHAYAVYITLS 660  
QY 661 IGAOTDFLSVPFSGYTFKHKWYVDLTLPESGEYFVMSNBNGLMILCCNHSDFRNG 720  
DB 661 IGAOTDFLSVPFSGYTFKHKWYVDLTLPESGEYFVMSNBNGLMILCCNHSDFRNG 720  
QY 721 MTALLKSSCDKNWGDYEDYEDISAYLLSKNNAIEPESFSONSRHPTROKQFNATTI 780  
DB 721 MTALLKSSCDKNWGDYEDYEDISAYLLSKNNAIEPESFSONSRHPTROKQFNATTI 780  
QY 781 PENDIEKTPDWFRAHRTPMFKIONVSSDLMLRQSPPHGLSLSDLOEAKYTFSDPS 840  
DB 781 PENDIEKTPDWFRAHRTPMFKIONVSSDLMLRQSPPHGLSLSDLOEAKYTFSDPS 840  
QY 841 PGALDSNNSLSEKTHFRQLHSGDWYTFPESGLQLRLNEKLTGTAATELKKLDFVYST 900  
DB 841 PGALDSNNSLSEKTHFRQLHSGDWYTFPESGLQLRLNEKLTGTAATELKKLDFVYST 900  
QY 901 SNNLITPTSDNLAAGTNTSLGPPSPVHYDSQDLDTLPFGKSSPLTESGGPLSLSEE 960  
DB 901 SNNLITPTSDNLAAGTNTSLGPPSPVHYDSQDLDTLPFGKSSPLTESGGPLSLSEE 960  
QY 961 NNDKSLLESGLNMSOESSGKNVSTFSGRLFGKRAHGPALLTFTDNALTFVYSISLKTN 1020  
DB 961 NNDKSLLESGLNMSOESSGKNVSTFSGRLFGKRAHGPALLTFTDNALTFVYSISLKTN 1020  
QY 1021 KTSNNSATNKKTHIDQPSLLIENSPSWQNIIESDPEFKYTPILHDBRLMDKNALRL 1080  
DB 1021 KTSNNSATNKKTHIDQPSLLIENSPSWQNIIESDPEFKYTPILHDBRLMDKNALRL 1080  
QY 1081 NMSNKTSTSSKNMEOVKKEGP1PPDAONPDMSPFKMLTFPESARW1ORTHKNSLNSG 1140  
DB 1081 NMSNKTSTSSKNMEOVKKEGP1PPDAONPDMSPFKMLTFPESARW1ORTHKNSLNSG 1140  
QY 1141 QGSPKQVLSLGEPEKSEGOVNFLEBKKNVYVGGEPTKDVGLKEVFPSSRNILFTNLND 1200  
DB 1141 QGSPKQVLSLGEPEKSEGOVNFLEBKKNVYVGGEPTKDVGLKEVFPSSRNILFTNLND 1200  
QY 1201 LHENNTNOKKTOEBTEKKEYLLOENVVLPOLHTYTGKRNKMLPLLSRONVEGSD 1260  
DB 1201 LHENNTNOKKTOEBTEKKEYLLOENVVLPOLHTYTGKRNKMLPLLSRONVEGSD 1260  
QY 1261 GAYAPVLQDFRSLNDSNTNKKHTAHFSKKGEBENLEGLNQTQOYERKYACTRISPT 1320  
DB 1261 GAYAPVLQDFRSLNDSNTNKKHTAHFSKKGEBENLEGLNQTQOYERKYACTRISPT 1320  
QY 1321 SOONFVTOQS-KRALQOFRLPLEETELEKRIYDDSTQMSKNMKMLPLPSYLOIYNEK 1379  
DB 1321 SOONFVTOQS-KRALQOFRLPLEETELEKRIYDDSTQMSKNMKMLPLPSYLOIYNEK 1379  
QY 1380 EKGATIOSPLSDCLTFPSHSIPDANRSPPLAKYSSPSTIRPYTLRLVLPDONSHTLPAAS 1439  
DB 1380 EKGATIOSPLSDCLTFPSHSIPDANRSPPLAKYSSPSTIRPYTLRLVLPDONSHTLPAAS 1439  
QY 1440 YRKDSCVOSSHFTLOGAKKNLSLILTEMTGDORREVSLGTSATNSVTYKVENYVL 1499  
DB 1440 YRKDSCVOSSHFTLOGAKKNLSLILTEMTGDORREVSLGTSATNSVTYKVENYVL 1499  
QY 1500 PKPDLPTSGVYELPKVHIYOKDLFTETSNQSPGHDLVBSLLAQTEGATIKWNEAR 1559  
DB 1500 PKPDLPTSGVYELPKVHIYOKDLFTETSNQSPGHDLVBSLLAQTEGATIKWNEAR 1559  
QY 1560 PKGVPFLRVATESSATPSKLLDPLANDNHYGNQIFKEEMKQGEKSPKTAFAKKKDTIIS 1619  
DB 1560 PKGVPFLRVATESSATPSKLLDPLANDNHYGNQIFKEEMKQGEKSPKTAFAKKKDTIIS 1619

D	1561	PGKVPFLRVATSSAKTSKLLDPLADWNHYGQIQPREEMKSOEKSPKTAFFKKKDTLLS	1620
Q	1620	LNACSNHAIATAINEGONKPELEVTMAKOGTRRLCSOMPVLAKHOREITRTTLOSDE	1679
D	1621	LNACSNHAIATAINEGONKPELEVTMAKOGTRRLCSOMPVLAKHOREITRTTLOSDE	1680
Q	1680	EIDYDDTISYEAKKKEFDIYDENOSPRFOKKTHTHTIAVENLMDYGMSSPHYLN	1739
D	1681	EIDYDDTISYEAKKKEFDIYDENOSPRFOKKTHTHTIAVENLMDYGMSSPHYLN	1740
Q	1740	RAQSGSVPOFKKVVQEFETDGSFTQPLRGELNENHGLGPIRAVEEDNIMVTFRNAS	1799
D	1741	RAQSGSVPOFKKVVQEFETDGSFTQPLRGELNENHGLGPIRAVEEDNIMVTFRNAS	1800
Q	1800	RPYSFYSLSIYEDDROGAEPKRNFKPNETKTYFMKVQHMAPTKDEPCKRAMAYFSD	1859
D	1801	RPYSFYSLSIYEDDROGAEPKRNFKPNETKTYFMKVQHMAPTKDEPCKRAMAYFSD	1860
Q	1860	VDLEKDVHSLGIPLLVCHTNTLPAHGRQVYQERFALFTTEDTKSWTFTEMERKCR	1919
D	1861	VDLEKDVHSLGIPLLVCHTNTLPAHGRQVYQERFALFTTEDTKSWTFTEMERKCR	1920
Q	1920	APCNIMDEPTEFKENRPHAINGYIMDTLPGLVMAODRIRWYLLSMGSNENIHSIHFSG	1979
D	1921	APCNIMDEPTEFKENRPHAINGYIMDTLPGLVMAODRIRWYLLSMGSNENIHSIHFSG	1980
Q	1980	HFTVVRKKEEYKMAALYNLYPGVFETEMLPKSKAGIRVCECLGELHAGMSTFLVLYSNK	2039
D	1981	HFTVVRKKEEYKMAALYNLYPGVFETEMLPKSKAGIRVCECLGELHAGMSTFLVLYSNK	2040
Q	2040	CQPLGMAASHINDRQITNASGYQGNAPKLARLHSGSINAMSTSEPPSWATKVDLAPMT	2099
D	2041	CQPLGMAASHINDRQITNASGYQGNAPKLARLHSGSINAMSTSEPPSWATKVDLAPMT	2100
Q	2100	IHGKIQGAKOKFSSLYISQFLIMYSLDGKWKQOTYRGNSTGLMVFEGNDSSGIRKHNIF	2159
D	2101	IHGKIQGAKOKFSSLYISQFLIMYSLDGKWKQOTYRGNSTGLMVFEGNDSSGIRKHNIF	2160
Q	2160	NPPIIARYIRLAPTHHSIRSLRMEIMGCDLNCSPMLMESKASIDQITASSYFTNMF	2219
D	2161	NPPIIARYIRLAPTHHSIRSLRMEIMGCDLNCSPMLMESKASIDQITASSYFTNMF	2220
Q	2220	ATWSPKARLHLOGRENAROVNPKEMLOVDPOKTMKVTVGTQGVKSLTSMYKKE	2279
D	2221	ATWSPKARLHLOGRENAROVNPKEMLOVDPOKTMKVTVGTQGVKSLTSMYKKE	2280
Q	2280	LISSSDGQHWTLFPQNGKVKVFGQNDSETPVYNSLDPPLLRRLRTHPOSWVHQTALR	2339
D	2281	LISSSDGQHWTLFPQNGKVKVFGQNDSETPVYNSLDPPLLRRLRTHPOSWVHQTALR	2340
Q	2340	MEVLGCEADODLY 2351	
D	2341	MEVLGCEADODLY 2352	

## RESULT 45

ID	AAW11406	standard; Protein: 2352 AA.
AC	AAW11406;	
XX	20-NOV-1997	(first entry)
DE	Active Factor VIII:C analogue residue 776 P Insertion.	
XX	Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;	
KM	fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;	
KM	plasma protease; thrombin; immunogen; antibody; haemophiliaac; therapy;	
XX	proteolytic cleavage.	
OS	Homo sapiens.	
OS	Synthetic.	

XX	Key	Location/Qualifiers
PH	Peptide	1..19
FT	Protein	/note= "signal peptide"
FT	Region	20..2352
FT	Region	/note= "mature Factor VIII:C"
FT	Misc-difference	20..1668
FT	Region	/note= "heavy chain fragment"
FT	Region	/note= "inserted residue"
FT	Domain	/note= "light chain fragment"
FT	Domain	/note= "B domain"
PD	30-JAN-1997.	
XX	09-JUL-1996;	96NC-US11444.
XX	11-JUL-1995;	95US-0001025.
XX	(CHIR ) CHIRON CORP.	
XX	Cohen FE, Hung DT, Innis M;	
XX	WPI; 1997-119050/11.	
XX	Factor VIII:C analog modified adjacent to a non-activating Arg	
PT	residue - used in the treatment of haemophilias, by improvement of	
PT	haemostasis	
PS	Claim 25; Page -; 90pp; English.	
XX	AAW11330-W1472 represent active Factor VIII:C analogues of the	
CC	invention. These sequences were created by mutating the wild type Factor	
CC	VIII:C coding sequence (see AAT51357) using mutagenic primers. The	
CC	analogues comprise a native Factor VIII:C polypeptide modified at a site	
CC	adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg	
CC	dipeptide is created. Factor VIII:C is a large glycoprotein that	
CC	participates in the blood coagulation cascade that ultimately converts	
CC	soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A	
CC	deficiency in Factor VIII:C is responsible for haemophilia A, which is an	
CC	X-chromosome linked inherited bleeding diathesis. Factor VIII:C is	
CC	activated by plasma proteases, such as thrombin. During activation the	
CC	mature polypeptide is cleaved to generate heavy and light chain fragments	
CC	that are further cleaved. Complexes of two or more of the analogues,	
CC	nucleic acids and vectors encoding them may be used alone or in	
CC	conjunction with each other, for the prevention or treatment of active	
CC	Factor VIII:C deficiency in a mammal. The analogues may be used as	
CC	immunogens to raise antibodies, and in the treatment of haemophilias, by	
CC	improvement of haemostasis. The analogues are resistant to proteolytic	
CC	cleavage and display increased plasma half-life. They may be administered	
CC	at lower dosages and by different modes of administration.	
XX	Sequence 2352 AA.	
SO	Query Match	99.9%; Score 12407.5; DB 18; Length 2352;
	Best Local Similarity	100.0%; Pred. No. 0;
	Matches 2351; Conservative	0; Mismatches 0; Indels 1; Gaps 1;
Q	1	MQELSTCFPLCLRFCSATRRYRLGAVELSDVWQSDLGELPVDARPPRPVKSFPFN 60
D	1	MQELSTCFPLCLRFCSATRRYRLGAVELSDVWQSDLGELPVDARPPRPVKSFPFN 60
Q	61	TSVYRKTLTFVEPTDHLNIAKPPPMGLGTTQAEVYQTVYTTKNAASHPVSLAHV 120
D	61	TSVYRKTLTFVEPTDHLNIAKPPPMGLGTTQAEVYQTVYTTKNAASHPVSLAHV 120
Q	121	GVSYWKASBGAEDYDQTSQREKEDKVPFGSHYVWVYLKENGPMASDPLCLTYSYLSH 180
D	121	GVSYWKASBGAEDYDQTSQREKEDKVPFGSHYVWVYLKENGPMASDPLCLTYSYLSH 180

181 VDLKDLNSGLGALLVOCREGSLAKEKJOTLHKFLLFAFVDECKSWHSETKNSLMODRD 240  
181 VDLKDLNSGLGALLVOCREGSLAKEKJOTLHKFLLFAFVDECKSWHSETKNSLMODRD 240  
181 VDLKDLNSGLGALLVOCREGSLAKEKJOTLHKFLLFAFVDECKSWHSETKNSLMODRD 240  
241 AASARAPKMHRTVNGYVNRSLPGLICGHRKSYVMHVIGMGTTPVHSLFLEGHTFLVRNH 300  
241 AASARAPKMHRTVNGYVNRSLPGLICGHRKSYVMHVIGMGTTPVHSLFLEGHTFLVRNH 300  
241 AASARAPKMHRTVNGYVNRSLPGLICGHRKSYVMHVIGMGTTPVHSLFLEGHTFLVRNH 300  
301 ROASLEISPTFLTAQTLMDLGOFLFCHISSHODGMEAYVAVDSCPEEPOLRKNNE 360  
301 ROASLEISPTFLTAQTLMDLGOFLFCHISSHODGMEAYVAVDSCPEEPOLRKNNE 360  
301 ROASLEISPTFLTAQTLMDLGOFLFCHISSHODGMEAYVAVDSCPEEPOLRKNNE 360  
361 EADYDDDLTJSEMDVYVTPHSDNSPFIQIRSAKHKHKTVMHYIAAEEDMDYAFIYA 420  
361 EADYDDDLTJSEMDVYVTPHSDNSPFIQIRSAKHKHKTVMHYIAAEEDMDYAFIYA 420  
361 EADYDDDLTJSEMDVYVTPHSDNSPFIQIRSAKHKHKTVMHYIAAEEDMDYAFIYA 420  
421 PDDRYSKQYLMNGFORIGRKYKKVRPMAYVDETEKTRBAIQHBSGILGFLYGEVDTL 480  
421 PDDRYSKQYLMNGFORIGRKYKKVRPMAYVDETEKTRBAIQHBSGILGFLYGEVDTL 480  
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541 TKSDPRCLTRYSSSVNNEBDLASGLIGPLLCYKESVDONGNOIMSDKRNVLFSVEDE 600  
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601 NRSWYLTENIQRFLEPNPAGVQLEDEPEFOASNIHSHINGYVDSIQLSVCLHEAVAYIILS 660  
601 NRSWYLTENIQRFLEPNPAGVQLEDEPEFOASNIHSHINGYVDSIQLSVCLHEAVAYIILS 660  
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1320 TSOQNVYTRSKRALQKRLPLEETLEKRIYVDOTSTONSKNNKHLTPSTLOIDYNEK 1379  
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2340 MEVLGCEPADLY 2351

Db 2341 MEVLSCPADLX 2352

RESULT 46  
AAW1407  
ID AAW1407 standard; Protein; 2352 AA.  
AC AAW1407;  
XX  
XX 20-NOV-1997 (first entry)  
DE Active Factor VIII:C analogue residue 777 P insertion.  
XX  
XX Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;  
KM fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KM plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;  
XX proteolytic cleavage.  
XX  
OS Homo sapiens.  
XX Synthetic.  
FH Key Location/Qualifiers  
FT Peptide 1..19  
FT /note= "signal peptide"  
FT Protein 20..2352  
FT /note= "mature Factor VIII:C"  
FT Region 20..1668  
FT /note= "heavy chain fragment"  
FT Misc-difference 796  
FT /note= "inserted residue"  
FT Region 1669..2351  
FT /note= "light chain fragment"  
FT Domain 761..1668  
FT /note= "B domain"  
XX  
XX WO9703195-A1.  
XX  
XX 30-JAN-1997.  
XX  
XX 09-JUL-1996; 96WO-US11444.  
XX  
XX 11-JUL-1995; 95US-0001025.  
XX  
XX (CHIR ) CHIRON CORP.  
XX  
XX Cohen FE, Hung DT, Innis M;  
XX  
XX WPI: 1997-119050/11.  
XX  
XX Factor VIII:C analog modified adjacent to a non-activating Arg  
XX residue - used in the treatment of haemophilias, by improvement of  
XX haemostasis  
XX  
XX Claim 25; Page -: 90pp; English.  
XX  
XX AAW1330-W11472 represent active Factor VIII:C analogues of the  
XX invention. These sequences were created by mutating the wild type Factor  
XX VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
XX analogues comprise a native Factor VIII:C polypeptide modified at a site  
XX adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
XX dipeptide is created. Factor VIII:C is a large glycoprotein that  
XX participates in the blood coagulation cascade that ultimately converts  
XX soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
XX deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
XX X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
XX activated by plasma proteases, such as thrombin. During activation the  
XX mature polypeptide is cleaved to generate heavy and light chain fragments  
XX that are further cleaved. Complexes of two or more of the analogues,  
XX nucleic acids and vectors encoding them may be used alone or in  
XX conjunction with each other, for the prevention or treatment of active  
XX Factor VIII:C deficiency in a mammal. The analogues may be used as  
XX immunogens to raise antibodies, and in the treatment of haemophilias, by

CC Improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX

SO Sequence 2352 AA;

Query Match 99.9%; Score 12407.5; DB 18; Length 2352;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

QY 1 MQIELSTCFCLLPFCFSATRRYYLGAELSDMDQSDLCLEPVDARPPRVKSPFN 60  
DB 1 MQIELSTCFCLLPFCFSATRRYYLGAELSDMDQSDLCLEPVDARPPRVKSPFN 60  
QY TSVYKKTLEFETDHLFNIAKRPMPMGLPTIOAEVDTVYITLKMAHPVSLHAV 120  
DB TSVYKKTLEFETDHLFNIAKRPMPMGLPTIOAEVDTVYITLKMAHPVSLHAV 120  
QY 61 TSVYKKTLEFETDHLFNIAKRPMPMGLPTIOAEVDTVYITLKMAHPVSLHAV 120  
DB 61 TSVYKKTLEFETDHLFNIAKRPMPMGLPTIOAEVDTVYITLKMAHPVSLHAV 120  
QY 121 GSVYKASGAEYDDQTSQREKEDKVPFGSGSHYVVOYLKENGPMASDPLCLTYSLH 180  
DB 121 GSVYKASGAEYDDQTSQREKEDKVPFGSGSHYVVOYLKENGPMASDPLCLTYSLH 180  
QY 121 VDLVKNLSGLIGALLVCBSGLAKEKTOYTLKFTLLFAVDECKSNHSTKNSLMODR 240  
DB 121 VDLVKNLSGLIGALLVCBSGLAKEKTOYTLKFTLLFAVDECKSNHSTKNSLMODR 240  
QY 241 AASARAMPKMTVNGVYVRSPLGLICGHRKSYVMHVIQMTPEVHSIFLEGHTFLVRNH 300  
DB 241 AASARAMPKMTVNGVYVRSPLGLICGHRKSYVMHVIQMTPEVHSIFLEGHTFLVRNH 300  
QY 301 ROASLEISPTFTLQTLMDLQGLFCHISHOHDMEMVYVDSCEPEPLRKKNNE 360  
DB 301 ROASLEISPTFTLQTLMDLQGLFCHISHOHDMEMVYVDSCEPEPLRKKNNE 360  
QY 361 EABDYDDLTDSEMDVYREFDDNSPSFTQIRSAKHKRTVWHYIAAEEDMDYAPLYLA 420  
DB 361 EABDYDDLTDSEMDVYREFDDNSPSFTQIRSAKHKRTVWHYIAAEEDMDYAPLYLA 420  
QY 421 PDDRSYKSOYLNNQFORIGRKYKVPVMTYETEPKTEALQHSGLIGPLXGEVDTL 480  
DB 421 PDDRSYKSOYLNNQFORIGRKYKVPVMTYETEPKTEALQHSGLIGPLXGEVDTL 480  
QY 481 LIIFKQASRPYNIYPHGITDVRPLYSRRLPGVKNHLKOPFLPGLFETKKTVYVEDGP 540  
DB 481 LIIFKQASRPYNIYPHGITDVRPLYSRRLPGVKNHLKOPFLPGLFETKKTVYVEDGP 540  
QY 541 TKSDPRCLTRYYSFVNMERDLASGLIGPLLCYKESVDQGNQIMSKRNVILFSVDE 600  
DB 541 TKSDPRCLTRYYSFVNMERDLASGLIGPLLCYKESVDQGNQIMSKRNVILFSVDE 600  
QY 601 NRSWYLTENIOEFLPNPAVOLEDPFOASNIMHSINGYVDSIQLSVCLHEVAYWYILS 660  
DB 601 NRSWYLTENIOEFLPNPAVOLEDPFOASNIMHSINGYVDSIQLSVCLHEVAYWYILS 660  
QY 661 IGAQDTFLSVFSGYTEKHKMYEDTLTLPFSGETVPMSENFGMLILCHNSDRNRG 720  
DB 661 IGAQDTFLSVFSGYTEKHKMYEDTLTLPFSGETVPMSENFGMLILCHNSDRNRG 720  
QY 721 MFLKLVSSCDNEDDYEDSYEDISAYLSKNNALIEFRSFSQSRHPTROKOFNATTI 780  
DB 721 MFLKLVSSCDNEDDYEDSYEDISAYLSKNNALIEFRSFSQSRHPTROKOFNATTI 780  
QY 781 PENDIKTDPWFARH-TPMKIOWSSSOLMLLKQSTTPRGISLSDOEAKYFSPDP 839  
DB 781 PENDIKTDPWFARH-TPMKIOWSSSOLMLLKQSTTPRGISLSDOEAKYFSPDP 839  
QY 840 SPDAIDNNSLSEMTHERPOLIHSNGDMVTTPESGLOLELNKELGTTAATLKKLPFKVSS 899  
DB 840 SPDAIDNNSLSEMTHERPOLIHSNGDMVTTPESGLOLELNKELGTTAATLKKLPFKVSS 899  
QY 900 TSNNTLSTPSONLAAGDMTSSLAGPSMPVHYDSQDPTLTFGKSSPLTEGGGLSISE 959  
DB 901 TSNNTLSTPSONLAAGDMTSSLAGPSMPVHYDSQDPTLTFGKSSPLTEGGGLSISE 960



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Qy 960 ENNDKLLLESGLMNSOESSMCKNVSSTPESGRLEFGKRAHGPALLLRKDALPKFVSIILKT 1019
    |||||
Db 961 ENNDKLLLESGLMNSOESSMCKNVSSTPESGRLEFGKRAHGPALLLRKDALPKFVSIILKT 1020
Qy 1020 NKTNSNATNRKTHIDGPSLTIENSPYWNILBSDETKKYTPLIHDMIMDKNATALR 1079
    |||||
Db 1021 NKTNSNATNRKTHIDGPSLTIENSPYWNILBSDETKKYTPLIHDMIMDKNATALR 1080
Qy 1080 LNHSNKTSTSSKNMEVQCKEGPIPPDAQNPDMSPFKMLFLPRESARNIORTHGKNSLNS 1139
    |||||
Db 1081 LNHSNKTSTSSKNMEVQCKEGPIPPDAQNPDMSPFKMLFLPRESARNIORTHGKNSLNS 1140
Qy 1140 GGGSPKOLVSLGPEKSVGONFLSEKKVYVNGGETDYGKEMVPPSSRNILFLTNLD 1199
    |||||
Db 1141 GGGSPKOLVSLGPEKSVGONFLSEKKVYVNGGETDYGKEMVPPSSRNILFLTNLD 1200
Qy 1200 NLHENMTHNOEKKIOEIEKKEFTLLIOENVYLPOIHVYTGKNEPMKLEFLSTRONVGSY 1259
    |||||
Db 1201 NLHENMTHNOEKKIOEIEKKEFTLLIOENVYLPOIHVYTGKNEPMKLEFLSTRONVGSY 1260
Qy 1260 DGAYAPVLODFRSLANDSTNRTKKTHTAHFSKKGEENLEGLNQTOIYEKTACTTRISPN 1319
    |||||
Db 1261 DGAYAPVLODFRSLANDSTNRTKKTHTAHFSKKGEENLEGLNQTOIYEKTACTTRISPN 1320
Qy 1320 TSOONFVTOBSKRALQOPRLPLETELEKRIYVDOTSTQSKNMKHLTPSTLQIDYNEK 1379
    |||||
Db 1321 TSOONFVTOBSKRALQOPRLPLETELEKRIYVDOTSTQSKNMKHLTPSTLQIDYNEK 1380
Qy 1380 EKGAIQSPISDCLTRSHSIPQANRSLPIAKVSSPISPIRYLIRVLEFQDNSSHLPAAS 1439
    |||||
Db 1381 EKGAIQSPISDCLTRSHSIPQANRSLPIAKVSSPISPIRYLIRVLEFQDNSSHLPAAS 1440
Qy 1440 YRKKGSGVOESSHFLGAKKNLSLAILTEMTDQDEKSGTSTANSVYKKEVNTVL 1499
    |||||
Db 1441 YRKKGSGVOESSHFLGAKKNLSLAILTEMTDQDEKSGTSTANSVYKKEVNTVL 1500
Qy 1500 PKPOLPKTSKVELLKXVHLYOKOLFPTETNSGSPGHLDYBSULQSTEGATKNENANR 1559
    |||||
Db 1501 PKPOLPKTSKVELLKXVHLYOKOLFPTETNSGSPGHLDYBSULQSTEGATKNENANR 1560
Qy 1560 PGKVPFLRVATESSAKTPSKLLDPLAMDNHYGTQIPKEEKSOEKSPEKTAFFKKDITLS 1619
    |||||
Db 1561 PGKVPFLRVATESSAKTPSKLLDPLAMDNHYGTQIPKEEKSOEKSPEKTAFFKKDITLS 1620
Qy 1620 LNACESNHAIATAINEGONKPEIEYTWAKOGTEBLCSQNPVLYKRRHORETRTLOSDOE 1679
    |||||
Db 1621 LNACESNHAIATAINEGONKPEIEYTWAKOGTEBLCSQNPVLYKRRHORETRTLOSDOE 1680
Qy 1680 EIDIDDTISVBMKKEPDIIYDEENQSPRSFOKTRHYFTAAVERLMDYGSSSPHYLRN 1739
    |||||
Db 1681 EIDIDDTISVBMKKEPDIIYDEENQSPRSFOKTRHYFTAAVERLMDYGSSSPHYLRN 1740
Qy 1740 RAQSGSVPOFKKVVFOEFTDGSFTQPLRGELNHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
    |||||
Db 1741 RAQSGSVPOFKKVVFOEFTDGSFTQPLRGELNHLGLLGPYIRAEVEDNIMVTFRNQAS 1800
Qy 1800 RPYSFYSLSIYEEDROGAPRKKNPVKNETKTYFKWKNONHNAAPKDEFOCKAAAFSD 1859
    |||||
Db 1801 RPYSFYSLSIYEEDROGAPRKKNPVKNETKTYFKWKNONHNAAPKDEFOCKAAAFSD 1860
Qy 1860 VDLEKDVHSGLIGPLVCHTNFLNPAHGRVTVQEFALFTIIDEFKSYFTEMMERNCR 1919
    |||||
Db 1861 VDLEKDVHSGLIGPLVCHTNFLNPAHGRVTVQEFALFTIIDEFKSYFTEMMERNCR 1920
Qy 1920 APCNIOMEDPTEFKENTRFHAINGYIMDTPLGIVAAQORIRWYLLSMGSENEIHSIHPSG 1979
    |||||
Db 1921 APCNIOMEDPTEFKENTRFHAINGYIMDTPLGIVAAQORIRWYLLSMGSENEIHSIHPSG 1980
Qy 1980 HYFTYRKKKEEKKAALYLLPGVPEYVEMLPKSAITRVYECULTEGHLHAAMSTLFLVYSNK 2039
    |||||
Db 1981 HYFTYRKKKEEKKAALYLLPGVPEYVEMLPKSAITRVYECULTEGHLHAAMSTLFLVYSNK 2040

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Qy 2040 CQPLGNMASHIRDPQITASGOYGOMAPKLARLHYSGSINAMSTKEPESWIKVDLAPMI 2099
    |||||
Db 2041 CQPLGNMASHIRDPQITASGOYGOMAPKLARLHYSGSINAMSTKEPESWIKVDLAPMI 2100
Qy 2100 IHGIKTGAQAKQSSLYISQFIIMSLDGKKWQYVRNNSGTLMPFQGVNDSGIKHNIF 2159
    |||||
Db 2101 IHGIKTGAQAKQSSLYISQFIIMSLDGKKWQYVRNNSGTLMPFQGVNDSGIKHNIF 2160
Qy 2160 NPPIIARYIRLHPHTHYSIRSTLRMELMCDLNSCSMPLEKSKAISDAQITASSYFTNMF 2219
    |||||
Db 2161 NPPIIARYIRLHPHTHYSIRSTLRMELMCDLNSCSMPLEKSKAISDAQITASSYFTNMF 2220
Qy 2220 ATWSPSKARLHLGGRNAMPQVNNPKEMLOVDROKTMKYTGVTQGYKSLTSMYKEF 2279
    |||||
Db 2221 ATWSPSKARLHLGGRNAMPQVNNPKEMLOVDROKTMKYTGVTQGYKSLTSMYKEF 2280
Qy 2280 LISSQDGHQWTLFQNGKVKYVQGNDSFTPPVNSLDPELTLRYLRHPOSWHQIALR 2339
    |||||
Db 2281 LISSQDGHQWTLFQNGKVKYVQGNDSFTPPVNSLDPELTLRYLRHPOSWHQIALR 2340
Qy 2340 MEVLGCEADOLY 2351
    |||||
Db 2341 MEVLGCEADOLY 2352

RESULT 47
AA011412
ID AA011412 standard; Protein; 2352 AA.
XX
AC AA011412;
XX
DT 20-NOV-1997 (first entry)
XX
DE Active Factor VIII:C analogue residue 775 F/E/P insertion.
XX
KW Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW plasma protease; thrombin; immunogen; antibody; haemophilia; therapy;
KW proteolytic cleavage.
XX
OS Homo sapiens.
OS synthetic.
XX
FH Peptide
FT 1..19 location/Qualifiers
FT /note= "signal peptide"
FT 20..2352
FT /note= "mature Factor VIII:C"
FT 20..1668
FT Region
FT /note= "heavy chain fragment"
FT 794
FT /label= "Phe, Glu, Pro"
FT /note= "inserted residue"
FT 1669..2351
FT /note= "light chain fragment"
FT 760..1668
FT Domain
FT /note= "B domain"

MO9703195-A1.
PD 30-JAN-1997.
PF 09-JUL-1996; 96MO-US11444.
PR 11-JUL-1995; 95US-0001025.
PA (CHIR ) CHIRON CORP.
PI Cohen FE, Hung DT, Innis M;
DK WPI; 1997-119050/11.
XX Factor VIII:C analog modified adjacent to a non-activating Arg

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PT residue - used in the treatment of haemophilias, by improvement of  
PT haemostasis  
XX  
PS Claim 26; Page -: 90pp; English.

CC AAW1330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophilias, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.

SO Sequence 2352 AA;

Query Match 99.9%; Score 12407.5; DB 18; Length 2352;

Best Local Similarity 100.0%; Pred. No. 0; Indels 1; Gaps 1;

Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

QY 1 MQIELSTCFELCLRFCSATRRYYLGAVELSMWYQSDGLPYDANPRPRPKSPFN 60  
DB 1 MQIELSTCFELCLRFCSATRRYYLGAVELSMWYQSDGLPYDANPRPRPKSPFN 60  
QY 61 TSVYKKTLFEVETHLFNIAKPRPPMGLGPTIOAEVYDVVTTLKNMASHPSLHAY 120  
DB 61 TSVYKKTLFEVETHLFNIAKPRPPMGLGPTIOAEVYDVVTTLKNMASHPSLHAY 120  
QY 121 GSVYKWSAGAEYDQTSOREKEDDKYFGSGSTYYWOLKNGMADPCLTYSLSH 180  
DB 121 GSVYKWSAGAEYDQTSOREKEDDKYFGSGSTYYWOLKNGMADPCLTYSLSH 180  
QY 121 GSVYKWSAGAEYDQTSOREKEDDKYFGSGSTYYWOLKNGMADPCLTYSLSH 180  
DB 121 GSVYKWSAGAEYDQTSOREKEDDKYFGSGSTYYWOLKNGMADPCLTYSLSH 180  
QY 181 VDLVKDLSGLIGALLVCREGLAKERTQTLHKFILLFAVFDEGKSMHSETKNSLMODRD 240  
DB 181 VDLVKDLSGLIGALLVCREGLAKERTQTLHKFILLFAVFDEGKSMHSETKNSLMODRD 240  
QY 241 AASARAMPKHTYNGVNRSLPGLIGCHRSYVWHYIGGTTPEVHSIFLGGHFLVRNH 300  
DB 241 AASARAMPKHTYNGVNRSLPGLIGCHRSYVWHYIGGTTPEVHSIFLGGHFLVRNH 300  
QY 301 ROASLEISPTITFLTAOTLLMDGGLFCHSHSHOHDMGEMAYKVDSCPEEPLRMNNE 360  
DB 301 ROASLEISPTITFLTAOTLLMDGGLFCHSHSHOHDMGEMAYKVDSCPEEPLRMNNE 360  
QY 361 EAEYDDDLTDSMDVYRFDDDNSSFIQISYAKKHKPTWYHIAAEEBMDAPLVLA 420  
DB 361 EAEYDDDLTDSMDVYRFDDDNSSFIQISYAKKHKPTWYHIAAEEBMDAPLVLA 420  
QY 421 PDDRSYSQYLLNNGPQIRKTKKVRMAAYDETFKTREAIQHESSILGILLYGEVDTL 480  
DB 421 PDDRSYSQYLLNNGPQIRKTKKVRMAAYDETFKTREAIQHESSILGILLYGEVDTL 480  
QY 481 LIIFKNQASRPYNIYHGHTIDVRPLYSRLLPKGVKHLKDPILPGEIEFYKKTAVVEDGP 540  
DB 481 LIIFKNQASRPYNIYHGHTIDVRPLYSRLLPKGVKHLKDPILPGEIEFYKKTAVVEDGP 540  
QY 541 TKSPPCLTRYSSFFYNMERDLASGLIOPLLICTKESVDQRGQINMSKRNITLFSVDE 600  
DB 541 TKSPPCLTRYSSFFYNMERDLASGLIOPLLICTKESVDQRGQINMSKRNITLFSVDE 600  
QY 601 NRSWYLTENIQRFLLPMPAGVQLEDEPQASNMHSINGYFDSILQSLVCLHEAVWTLLS 660

DB 601 NRSWYLTENIQRFLLPMPAGVQLEDEPQASNMHSINGYFDSILQSLVCLHEAVWTLLS 660  
QY 661 IGAOTDPLSVFFSGYTFKHKMYEDTTLFPFSGETVFSMKNPGLMILGCHNSDFRNG 720  
DB 661 IGAOTDPLSVFFSGYTFKHKMYEDTTLFPFSGETVFSMKNPGLMILGCHNSDFRNG 720  
QY 721 MTALLKSSCDKNTGTYEDSDYEDISATLLSKNNAIEPRFSQNSRHSPTROKOFNATTI 780  
DB 721 MTALLKSSCDKNTGTYEDSDYEDISATLLSKNNAIEPRFSQNSRHSPTROKOFNATTI 780  
QY 781 PENDIEKTDMPFA-HRTPMKIQNYSSDLMILLROSPPRHGISLSDLOEAKYTFESDOP 839  
DB 781 PENDIEKTDMPFA-HRTPMKIQNYSSDLMILLROSPPRHGISLSDLOEAKYTFESDOP 840  
QY 840 SPGALDSNNSLSMTFPRROLHNSGDWYFPEGSLQRLNEKIGTTAATELKKLDPKVSS 899  
DB 841 SPGALDSNNSLSMTFPRROLHNSGDWYFPEGSLQRLNEKIGTTAATELKKLDPKVSS 900  
QY 900 TSNNLSTIPSDNLAAGTNTSSILGPPMPVHYDSQDLDTLLFGKSSPLTESGPLUSE 959  
DB 901 TSNNLSTIPSDNLAAGTNTSSILGPPMPVHYDSQDLDTLLFGKSSPLTESGPLUSE 960  
QY 960 ENDSKLLSGLMNSOESSGMKNVSTSGRLFGRKRAHPALLTRQNALPFVYSILTKT 1019  
DB 961 ENDSKLLSGLMNSOESSGMKNVSTSGRLFGRKRAHPALLTRQNALPFVYSILTKT 1020  
QY 1020 NKTSSNATNKRTHIDPSSLTENSPPWQNLSDTEFFKVTPLIHDRMLDKNATLRL 1079  
DB 1021 NKTSSNATNKRTHIDPSSLTENSPPWQNLSDTEFFKVTPLIHDRMLDKNATLRL 1080  
QY 1080 LNHMSNKTSSKNNEWQOKKEBIPDPAQNDMSFFKMLFEPESARWIOPTHNGKNSLNS 1139  
DB 1081 LNHMSNKTSSKNNEWQOKKEBIPDPAQNDMSFFKMLFEPESARWIOPTHNGKNSLNS 1140  
QY 1140 GGGSPKOLVSLGPKSVESQNFLESKKNVYVGGEFTKXVGLKEVPFSSNLETLTMD 1199  
DB 1141 GGGSPKOLVSLGPKSVESQNFLESKKNVYVGGEFTKXVGLKEVPFSSNLETLTMD 1200  
QY 1200 NLHENNTHNOEKKIOEIEIEKETTLOENVVLPOIHTYGTGKFMKMLPLSTROVDESY 1259  
DB 1201 NLHENNTHNOEKKIOEIEIEKETTLOENVVLPOIHTYGTGKFMKMLPLSTROVDESY 1260  
QY 1260 DCAVAPVLODPRSLNDSTNRTKHTHFKSKGEEENEGJONGQKOIVKCYACTRISP 1319  
DB 1261 DCAVAPVLODPRSLNDSTNRTKHTHFKSKGEEENEGJONGQKOIVKCYACTRISP 1320  
QY 1320 TSQONFVQSRKALAKOFLPELETELEKRIIVDDTSTQMSKMKHLTSTLTQIDYNEK 1379  
DB 1321 TSQONFVQSRKALAKOFLPELETELEKRIIVDDTSTQMSKMKHLTSTLTQIDYNEK 1380  
QY 1380 EKGATITQSPSLDCLTRSHSIPQANRSPILIAKVSFPIRITYLTRVLEFQDNSSHLPAAS 1439  
DB 1381 EKGATITQSPSLDCLTRSHSIPQANRSPILIAKVSFPIRITYLTRVLEFQDNSSHLPAAS 1440  
QY 1440 YRKDSGVQESSHFLQCAKKNNTSLAILLEMTGQQRVSGLSGTSAINSTYKYKENVYL 1499  
DB 1441 YRKDSGVQESSHFLQCAKKNNTSLAILLEMTGQQRVSGLSGTSAINSTYKYKENVYL 1500  
QY 1500 PKPDLPTSGVVELLPVHTIYQKDLPEPTSGSGSHGLDVEGSLLOGTGCAIKMNEANR 1559  
DB 1501 PKPDLPTSGVVELLPVHTIYQKDLPEPTSGSGSHGLDVEGSLLOGTGCAIKMNEANR 1560  
QY 1560 PGKVPPLVATESSAKTPSKULDPLAMDNHGTQTPREKMSQKSPSEKAPFKKDTLIS 1619  
DB 1561 PGKVPPLVATESSAKTPSKULDPLAMDNHGTQTPREKMSQKSPSEKAPFKKDTLIS 1620  
QY 1620 LNACESNHAIAINEGQNKPEIEVYTAQOGRTERLCSQNPVLKRHRQREITRTTLOSDE 1679  
DB 1621 LNACESNHAIAINEGQNKPEIEVYTAQOGRTERLCSQNPVLKRHRQREITRTTLOSDE 1680  
QY 1680 EIDYDDTISVEKKEDPDYIDDEQNSPPSPQKTRHETIAAVERLDWYSSPHVLN 1739

Db	1681	EIDVDPTISVEMKKEDFDIYDEDENOGSPRSFOKTRHNYIAAVERLMDYGMSSSPHYLN	1740
Qy	1740	RAQSGSVPOGKKVYDFEPTDGSFTPOPLRYREGLNEHILGLGPYIAEVEDNIMVTFPNQAS	1799
Db	1741	RAQSGSVPOGKKVYDFEPTDGSFTPOPLRYREGLNEHILGLGPYIAEVEDNIMVTFPNQAS	1800
Qy	1800	RPYFYSLSLISYEDROGAEPKRNKVPKPYETKYTWKVOHHMAPTDEDFCKAMAYFSD	1859
Db	1801	RPYFYSLSLISYEDROGAEPKRNKVPKPYETKYTWKVOHHMAPTDEDFCKAMAYFSD	1860
Qy	1860	VDLEKDVHSLGLEPRLVCHTNTLNPARGROYTVOEFALEFTTIFEBTSMWTFENMRNCR	1919
Db	1861	VDLEKDVHSLGLEPRLVCHTNTLNPARGROYTVOEFALEFTTIFEBTSMWTFENMRNCR	1920
Qy	1920	APCNIQMEDPTFENRFRPAINGYIMDTLPGLYMAODQIRWYLLSMGSMENHSHIFSG	1979
Db	1921	APCNIQMEDPTFENRFRPAINGYIMDTLPGLYMAODQIRWYLLSMGSMENHSHIFSG	1980
Qy	1980	HVFYVRKKEEYKALNLYPGVFETVEMLSKAGIMRWVCLGELHAGMSTLEFLYSNK	2039
Db	1981	HVFYVRKKEEYKALNLYPGVFETVEMLSKAGIMRWVCLGELHAGMSTLEFLYSNK	2040
Qy	2040	CQTPFGAASGHINDPITASGQYGMAPKLARLHYSGSINANSTKEPSPWIKYDLAPM	2099
Db	2041	CQTPFGAASGHINDPITASGQYGMAPKLARLHYSGSINANSTKEPSPWIKYDLAPM	2100
Qy	2100	IHGIRTOGAROKFSSLYISQFLIMVSLDGKKMOTYRGANSTGTLWVFEGNVDSGIRKNTF	2159
Db	2101	IHGIRTOGAROKFSSLYISQFLIMVSLDGKKMOTYRGANSTGTLWVFEGNVDSGIRKNTF	2160
Qy	2160	NPPITARIYRIHPHTHYSINSTLRMEMLGCDLNCSPMLMESKATSAQDTAASYPFTNMF	2219
Db	2161	NPPITARIYRIHPHTHYSINSTLRMEMLGCDLNCSPMLMESKATSAQDTAASYPFTNMF	2220
Qy	2220	ATWSPSKARLHLGSGSNARPOVNNPKEMLOVDFORTKMTYGVTOGYKSLTSMYVKEF	2279
Db	2221	ATWSPSKARLHLGSGSNARPOVNNPKEMLOVDFORTKMTYGVTOGYKSLTSMYVKEF	2280
Qy	2280	LISSSQGOCHOMTLFPONGKVKYKFGQNDSTFPVYNSLDPLLTRYLRIHPQSWHOIALR	2333
Db	2281	LISSSQGOCHOMTLFPONGKVKYKFGQNDSTFPVYNSLDPLLTRYLRIHPQSWHOIALR	2340
Qy	2340	MEVLCEAODLY 2351	
Db	2341	MEVLCEAODLY 2352	
RESULT 48			
AAAM11417	ID	AAAM11417 standard; Protein; 2352 AA.	
XX	XX	AAAM11417;	
AC	XX		
DT	DT	20-NOV-1997 (first entry)	
DE	DE	Active Factor VIII:C analogue residue 1310 P insertion.	
XX	XX		
KM	KM	Factor VIII:C analogue; glycoprotein; blood coagulation cascade;	
KW	KW	fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;	
KM	KM	plasma protease; thrombin; immunosis; antibody; haemophilicac; therapy;	
KW	KW	proteolytic cleavage.	
XX	XX		
OS	OS	Homo sapiens.	
XX	XX	Synthetic.	
FT	FT	Key	Location/Qualifiers
FT	FT	Peptide	1..19
FT	FT	Protein	/note="signal peptide"
FT	FT	Region	20..2352
FT	FT		/note="mature Factor VIII:C"
FT	FT		20..1668
FT	FT	Misc-difference	/note="heavy chain fragment"
FT	FT		1329

[illegible]

QY 301 ROASLEISPTFLTAOTLLMDJGFLFCHISQHDGMEAYKVUSCEPEQLMKNE 360  
| | | | |  
Db 301 ROASLEISPTFLTAOTLLMDJGFLFCHISQHDGMEAYKVUSCEPEQLMKNE 360  
QY 361 EAEYDDDLTDESDVYRFBDONSPEFQIRSVAKKHPRKTWVHYIAAEEEDMAYPLVA 420  
| | | | |  
Db 361 EAEYDDDLTDESDVYRFBDONSPEFQIRSVAKKHPRKTWVHYIAAEEEDMAYPLVA 420  
QY 421 PDDRSYKSQYLNNGPORGAKTKKRFMAAYDEFTKTRREALIOHESGILPLLXGEVDTL 480  
| | | | |  
Db 421 PDDRSYKSQYLNNGPORGAKTKKRFMAAYDEFTKTRREALIOHESGILPLLXGEVDTL 480  
QY 481 LIIFKNQASRPYNIYPHGITDVAPLYSRRLPGVKYHLKDPILLGELFKKTVTVEDGP 540  
| | | | |  
Db 481 LIIFKNQASRPYNIYPHGITDVAPLYSRRLPGVKYHLKDPILLGELFKKTVTVEDGP 540  
QY 541 TKSDFRCILTRYSSFFVMEDLASGLISPLICYESVDORGNOIMSDKRNVLTSVEDE 600  
| | | | |  
Db 541 TKSDFRCILTRYSSFFVMEDLASGLISPLICYESVDORGNOIMSDKRNVLTSVEDE 600  
QY 541 TKSDFRCILTRYSSFFVMEDLASGLISPLICYESVDORGNOIMSDKRNVLTSVEDE 600  
| | | | |  
Db 541 TKSDFRCILTRYSSFFVMEDLASGLISPLICYESVDORGNOIMSDKRNVLTSVEDE 600  
QY 601 NRSWYLTENIORFLPNBAGVQLEDPEFOASNIMHSINGYVDSIQLSVCLHEVAYVILS 660  
| | | | |  
Db 601 NRSWYLTENIORFLPNBAGVQLEDPEFOASNIMHSINGYVDSIQLSVCLHEVAYVILS 660  
QY 661 IGAOTDFLSVFFSGYTFKHKMYEDTLTFPFGSETVMSMENGLMILGCHNSDFRNG 720  
| | | | |  
Db 661 IGAOTDFLSVFFSGYTFKHKMYEDTLTFPFGSETVMSMENGLMILGCHNSDFRNG 720  
QY 661 IGAOTDFLSVFFSGYTFKHKMYEDTLTFPFGSETVMSMENGLMILGCHNSDFRNG 720  
| | | | |  
Db 661 IGAOTDFLSVFFSGYTFKHKMYEDTLTFPFGSETVMSMENGLMILGCHNSDFRNG 720  
QY 721 MTALLKVSCKDKNTRYEDSYEDISAYILSKNNAIEPRFSONSRRPSTRQOFNATTI 780  
| | | | |  
Db 721 MTALLKVSCKDKNTRYEDSYEDISAYILSKNNAIEPRFSONSRRPSTRQOFNATTI 780  
QY 721 MTALLKVSCKDKNTRYEDSYEDISAYILSKNNAIEPRFSONSRRPSTRQOFNATTI 780  
| | | | |  
Db 721 MTALLKVSCKDKNTRYEDSYEDISAYILSKNNAIEPRFSONSRRPSTRQOFNATTI 780  
QY 781 PENDIEKTDPMFAHRTMPKIONVSSDDLMLRLSPPHGLISLSDQEAKEYTFSDPS 840  
| | | | |  
Db 781 PENDIEKTDPMFAHRTMPKIONVSSDDLMLRLSPPHGLISLSDQEAKEYTFSDPS 840  
QY 841 PGALDSNNSLSBMTHFRQLHSDMWTFPEGSLQRLNEKLTGTTAATELKIDFVYST 900  
| | | | |  
Db 841 PGALDSNNSLSBMTHFRQLHSDMWTFPEGSLQRLNEKLTGTTAATELKIDFVYST 900  
QY 841 PGALDSNNSLSBMTHFRQLHSDMWTFPEGSLQRLNEKLTGTTAATELKIDFVYST 900  
| | | | |  
Db 841 PGALDSNNSLSBMTHFRQLHSDMWTFPEGSLQRLNEKLTGTTAATELKIDFVYST 900  
QY 901 SNNLISTIPSDMLAGTDNTSSLCPPSMVHYDSQLDLTLFEGKSSPLTEGCGPLISEE 960  
| | | | |  
Db 901 SNNLISTIPSDMLAGTDNTSSLCPPSMVHYDSQLDLTLFEGKSSPLTEGCGPLISEE 960  
QY 961 NNDKILLESGLMNSOESMGKNVSTSSGRLFGKRAHGPALITKDNALFVYSILKTN 1020  
| | | | |  
Db 961 NNDKILLESGLMNSOESMGKNVSTSSGRLFGKRAHGPALITKDNALFVYSILKTN 1020  
QY 1021 KTSNNSATNRKTHIDGSPSLIENSPLYWONILESDETEFKKVTPLIHDMLMDKNAATLRL 1080  
| | | | |  
Db 1021 KTSNNSATNRKTHIDGSPSLIENSPLYWONILESDETEFKKVTPLIHDMLMDKNAATLRL 1080  
QY 1081 NMSNKTTSKKNMENVQOKEGPIPPDAONPDMSFFKMLFPPESARWIORTHGKNSLNSG 1140  
| | | | |  
Db 1081 NMSNKTTSKKNMENVQOKEGPIPPDAONPDMSFFKMLFPPESARWIORTHGKNSLNSG 1140  
QY 1141 QGSPKQVLSLGPBKSVEGONFLSEKKVYVVGGEFTKDYGLKENVPFSSNNLFLTMDN 1200  
| | | | |  
Db 1141 QGSPKQVLSLGPBKSVEGONFLSEKKVYVVGGEFTKDYGLKENVPFSSNNLFLTMDN 1200  
QY 1201 LHEHNTHNOEKKIOEIEIKKETLIOENVVLPOLIHTVTGKNFMKMLFLSTRONVEGSD 1260  
| | | | |  
Db 1201 LHEHNTHNOEKKIOEIEIKKETLIOENVVLPOLIHTVTGKNFMKMLFLSTRONVEGSD 1260  
QY 1261 GAYAPVLODFRSLNDSTNFKTHAHFSKGEENLEGJGNDKOIWEKTACTRIISPNT 1320  
| | | | |  
Db 1261 GAYAPVLODFRSLNDSTNFKTHAHFSKGEENLEGJGNDKOIWEKTACTRIISPNT 1320  
QY 1321 SQONFTVO-RSKRALKOFRLPLEETELEKRIIVDDSTOWSKMKHLTPSTLTOIDYNEK 1379  
| | | | |  
Db 1321 SQONFTVO-RSKRALKOFRLPLEETELEKRIIVDDSTOWSKMKHLTPSTLTOIDYNEK 1380  
QY 1380 EKGAIITOSPLSDCLTRSHSIPQANRSPPLIAKVSSPFSIRPIYILTRVLFQDNSSHLPAAS 1439

Db 1381 EKGAIITOSPLSDCLTRSHSIPQANRSPPLIAKVSSPFSIRPIYILTRVLFQDNSSHLPAAS 1440  
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QY 1440 YRKKSQGVESSEHFLQKAKKNNLSIALITLEMGOOREGSLGTSATNSYTKVKEVTVL 1499  
| | | | |  
Db 1441 YRKKSQGVESSEHFLQKAKKNNLSIALITLEMGOOREGSLGTSATNSYTKVKEVTVL 1500  
QY 1500 PKPDLPTSGVYELLPRKHVIOKDLFPTETSNGPSGLDLVEGSLLOGBGAIKKNENAR 1559  
| | | | |  
Db 1501 PKPDLPTSGVYELLPRKHVIOKDLFPTETSNGPSGLDLVEGSLLOGBGAIKKNENAR 1560  
QY 1560 PGKVPPLRATSSAKTPESKILDLPLANDNYGTQIRKEEMKSOEKSEPKTAFFKKDTILS 1619  
| | | | |  
Db 1561 PGKVPPLRATSSAKTPESKILDLPLANDNYGTQIRKEEMKSOEKSEPKTAFFKKDTILS 1620  
QY 1620 LMACESNHAIAINEGONKPEIEYTMAKQRTERLCSQNPVLAKHORELTRILOSDOE 1679  
| | | | |  
Db 1621 LMACESNHAIAINEGONKPEIEYTMAKQRTERLCSQNPVLAKHORELTRILOSDOE 1680  
QY 1680 EIDYDPTISYEKKEDFDIYEDENQSPRSFOKTRHAYIAAVERLMDYGMSSSPHYLRN 1739  
| | | | |  
Db 1681 EIDYDPTISYEKKEDFDIYEDENQSPRSFOKTRHAYIAAVERLMDYGMSSSPHYLRN 1740  
QY 1740 RAQSGSVPOFKKVVQOETDGSFTQPLRBEIMENHGLGAPYIRAEVEDNIMVFRQAS 1799  
| | | | |  
Db 1741 RAQSGSVPOFKKVVQOETDGSFTQPLRBEIMENHGLGAPYIRAEVEDNIMVFRQAS 1800  
QY 1800 RPSFSYSLISYEEDROGAEBRKNFKNPNETKYTFWKVOHHAAPTQDEFCAMAYFSD 1859  
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Db 1801 RPSFSYSLISYEEDROGAEBRKNFKNPNETKYTFWKVOHHAAPTQDEFCAMAYFSD 1860  
QY 1860 VDLEKDVHSLIGLPLVCHTNTLNANHROVYTOERAFPTTFDEFKSMVTEEMENCR 1919  
| | | | |  
Db 1861 VDLEKDVHSLIGLPLVCHTNTLNANHROVYTOERAFPTTFDEFKSMVTEEMENCR 1920  
QY 1920 APCNIOEMEDPTFKENYRFHAINGYIMDTLPGLVMAODQIRIMVLLSMGSNENIHSIFSG 1979  
| | | | |  
Db 1921 APCNIOEMEDPTFKENYRFHAINGYIMDTLPGLVMAODQIRIMVLLSMGSNENIHSIFSG 1980  
QY 1980 HFTVFRKKEEYKMAILNLYPGVEFVEMLPSKAGIMVVECLIGEHLHAGMSTFLVYSNK 2039  
| | | | |  
Db 1981 HFTVFRKKEEYKMAILNLYPGVEFVEMLPSKAGIMVVECLIGEHLHAGMSTFLVYSNK 2040  
QY 2040 CQPLGMAASHINDFOITASGOYGMARLARLARLYSSITANSTKEPSPYIKVLDLAPMI 2099  
| | | | |  
Db 2041 CQPLGMAASHINDFOITASGOYGMARLARLARLYSSITANSTKEPSPYIKVLDLAPMI 2100  
QY 2100 IHGIRTOGAROKFESSLYISOETIMYSLDGKMWQTYRGNSTGTLMEVFGVNDSSGIKHNIF 2159  
| | | | |  
Db 2101 IHGIRTOGAROKFESSLYISOETIMYSLDGKMWQTYRGNSTGTLMEVFGVNDSSGIKHNIF 2160  
QY 2160 NPPIIARTIRLHPHYSINSTRLMELMGCDLNSGSMPLGMEKASIDAOITASSYFTNMF 2219  
| | | | |  
Db 2161 NPPIIARTIRLHPHYSINSTRLMELMGCDLNSGSMPLGMEKASIDAOITASSYFTNMF 2220  
QY 2220 ATWSPSKARLHLQGRSNAMRPVONNPKEMLOVDFOKTMKYVTGYTQGVKSLTSMYVEF 2279  
| | | | |  
Db 2221 ATWSPSKARLHLQGRSNAMRPVONNPKEMLOVDFOKTMKYVTGYTQGVKSLTSMYVEF 2280  
QY 2280 LSSSQDQHQWTLRFQNGKQKVVQNGOOSFPYVNSLDPLRLTRYLRIRIPQSWVQOIALR 2339  
| | | | |  
Db 2281 LSSSQDQHQWTLRFQNGKQKVVQNGOOSFPYVNSLDPLRLTRYLRIRIPQSWVQOIALR 2340  
QY 2340 MEVLGCEAODLY 2351  
| | | | |  
Db 2341 MEVLGCEAODLY 2352  
| | | | |  
RESULT 49  
AAW11418  
ID AAW11418 standard; Protein: 2352 AA.  
XX  
AC AAW11418:

XX 20-NOV-1997 (first entry)  
XX Active Factor VIII:C analogue residue 1311 P insertion.  
DE  
XX Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;  
KM fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KW plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;  
XX proteolytic cleavage.  
XX Homo sapiens.  
OS Synthetic.  
XX  
FH Key Location/Qualifiers  
FT Peptide 1..19 /note= "signal peptide"  
FT Protein 20..2352 /note= "mature Factor VIII:C"  
FT Region 20..1668 /note= "heavy chain fragment"  
FT Misc-difference 1330 /note= "inserted residue"  
FT Region 1669..2351 /note= "light chain fragment"  
FT Domain 761..1668 /note= "B domain"  
PN MO9703195-A1.  
PD 30-JAN-1997.  
PF 09-JUL-1996; 96MO-US11444.  
XX 11-JUL-1995; 95US-0001025.  
PR (CHIR ) CHIRON CORP.  
XX Cohen FE, Hung DT, Innis M;  
XX MPI: 1997-119050/11.  
XX  
XX Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophiliacs, by improvement of  
PT haemostasis  
XX  
PS Claim 27; Page -: 90pp; English.  
XX  
XX AAM11330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophiliacs, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX  
XX Sequence 2352 AA:  
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

OY 1 MOELSTCFPLCLLRFCFSATRRYVLAVELSDMYQMSDGLGELPYDAFRPPVKSPFFN 60  
DB 1 MOELSTCFPLCLLRFCFSATRRYVLAVELSDMYQMSDGLGELPYDAFRPPVKSPFFN 60  
OY 61 TSVYKKTLEVEETDHLFNIAKPRPMWGLGPTIOAEYDVTYITLKNASHVSLAHV 120  
DB 61 TSVYKKTLEVEETDHLFNIAKPRPMWGLGPTIOAEYDVTYITLKNASHVSLAHV 120  
OY 121 GVSYWKASGAEYDDQTSQREKEDDKVFPGGSHYVWQVLEKNGPMASDPCLTYSLSH 180  
DB 121 GVSYWKASGAEYDDQTSQREKEDDKVFPGGSHYVWQVLEKNGPMASDPCLTYSLSH 180  
OY 181 VDLKVDLNSGLIGALLVCREGSLAEKQTLHKRFLFVPEGKSWSEKNSLMDRD 240  
DB 181 VDLKVDLNSGLIGALLVCREGSLAEKQTLHKRFLFVPEGKSWSEKNSLMDRD 240  
OY 241 AASARAMPKMHVYGVNRSPLGLIGHRKSVWVHVGMTTPEVHSLFLEGHTFLVRNH 300  
DB 241 AASARAMPKMHVYGVNRSPLGLIGHRKSVWVHVGMTTPEVHSLFLEGHTFLVRNH 300  
OY 301 ROASLEISPTFLTAOTLLMDLGOFLRCHTSSHQDGMFAVYKVDSCPEEPOLRMKNE 360  
DB 301 ROASLEISPTFLTAOTLLMDLGOFLRCHTSSHQDGMFAVYKVDSCPEEPOLRMKNE 360  
OY 361 EAEDYDDDLTDSMDYVRFDONSSEFIQTISVAKKPKTKVHYIAAEDDMYAPLYLA 420  
DB 361 EAEDYDDDLTDSMDYVRFDONSSEFIQTISVAKKPKTKVHYIAAEDDMYAPLYLA 420  
OY 421 PDDRSKYQYLNNGPORIGRKYKKRFAAYTDEFKTRAIQHESGILGPLLGEVSDTL 480  
DB 421 PDDRSKYQYLNNGPORIGRKYKKRFAAYTDEFKTRAIQHESGILGPLLGEVSDTL 480  
OY 481 LTIFFNOSAPRYNIYHGTIDVRLPLYSRLPKGVKHLKDPPLPGEFIPFKYKTYVEDGP 540  
DB 481 LTIFFNOSAPRYNIYHGTIDVRLPLYSRLPKGVKHLKDPPLPGEFIPFKYKTYVEDGP 540  
OY 541 TKSDEPCLTRYSSPVNMEEDLASGLICPLLCKESVDORGNOIMSKRNYLFSVDE 600  
DB 541 TKSDEPCLTRYSSPVNMEEDLASGLICPLLCKESVDORGNOIMSKRNYLFSVDE 600  
OY 601 NRSWLTENIORFLPPAGVQLEDEPFOASIMHSINGVYFDSIQSLVCLHEVAYWYILS 660  
DB 601 NRSWLTENIORFLPPAGVQLEDEPFOASIMHSINGVYFDSIQSLVCLHEVAYWYILS 660  
OY 661 IGAOTDFLSVFESEGYTKRMYEDTLTFPFGSETVEMENRPGIMTIGCHNSDFNRNG 720  
DB 661 IGAOTDFLSVFESEGYTKRMYEDTLTFPFGSETVEMENRPGIMTIGCHNSDFNRNG 720  
OY 721 MTALLKVSQCDKNTGDYEDSYEDISAVLLSKNNAIEPRSFQNSRHPSTROKOFNATTI 780  
DB 721 MTALLKVSQCDKNTGDYEDSYEDISAVLLSKNNAIEPRSFQNSRHPSTROKOFNATTI 780  
OY 781 PENDEKTDPMFAHRPPMKIONVSSDPLMLLQSPTPHGLSLSDLOAKYEFSDPS 840  
DB 781 PENDEKTDPMFAHRPPMKIONVSSDPLMLLQSPTPHGLSLSDLOAKYEFSDPS 840  
OY 841 PCADISNNSLSEWTHRRPRLHSGDMVTFPSSGQLRLNKKLTAAATBLKDFKVSST 900  
DB 841 PCADISNNSLSEWTHRRPRLHSGDMVTFPSSGQLRLNKKLTAAATBLKDFKVSST 900  
OY 901 SNLITSTIPSDNLAAAGTNTSSLGPPSPVHYDSQDLDTLTFGKSSPLTESGSPLSSEE 960  
DB 901 SNLITSTIPSDNLAAAGTNTSSLGPPSPVHYDSQDLDTLTFGKSSPLTESGSPLSSEE 960  
OY 961 NNDKSLLESSGLMANSOESGMCKNVSTREGSLRPFKRRHAGPALLTKNALFFKYSILKTN 1020  
DB 961 NNDKSLLESSGLMANSOESGMCKNVSTREGSLRPFKRRHAGPALLTKNALFFKYSILKTN 1020  
OY 1021 KTSNNSATNRKTHIDGSSLILENSVMQNTLESDETEFKKVTPLIDRMLDKNATLRL 1080  
DB 1021 KTSNNSATNRKTHIDGSSLILENSVMQNTLESDETEFKKVTPLIDRMLDKNATLRL 1080

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OY 1081 NMSNKTSSKNMEMVOQKKEGP1PPDAQNPDMSFFKMLFLPESARW1QTRHGSKNLSNG 1140
    |||||
DB 1081 NMSNKTSSKNMEMVOQKKEGP1PPDAQNPDMSFFKMLFLPESARW1QTRHGSKNLSNG 1140
OY 1141 OGSPKOLVSLGPEKSVGONFLSEKNKVVYVKGFTVDVGLKMWPPSSRNLFLLNLND 1200
    |||||
DB 1141 OGSPKOLVSLGPEKSVGONFLSEKNKVVYVKGFTVDVGLKMWPPSSRNLFLLNLND 1200
OY 1201 LHNHTHNOEKKIOEIEKEKTELIOENVVLPOIHTVGTGKNFMKNLFLSTRONVGSYD 1260
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DB 1201 LHNHTHNOEKKIOEIEKEKTELIOENVVLPOIHTVGTGKNFMKNLFLSTRONVGSYD 1260
OY 1261 GAYAPYLODFSLNDSTNRKTKTAHPSKKGFEENLBEGLNOTQIYEKACTRISPMT 1320
    |||||
DB 1261 GAYAPYLODFSLNDSTNRKTKTAHPSKKGFEENLBEGLNOTQIYEKACTRISPMT 1320
OY 1321 SQONFVTOB-SKRALKOFRLPLEETELERK1IVDDTSTOWSKNNKHLPLSTLQIDYNEK 1379
    |||||
DB 1321 SQONFVTOB-SKRALKOFRLPLEETELERK1IVDDTSTOWSKNNKHLPLSTLQIDYNEK 1380
OY 1380 EKGAITQSPSLDCLTRHSITPOANRSP1PIAVYSSPSP1RPIYLTRVLFODNSSHLPAAS 1439
    |||||
DB 1381 EKGAITQSPSLDCLTRHSITPOANRSP1PIAVYSSPSP1RPIYLTRVLFODNSSHLPAAS 1440
OY 1440 YRKKGVOESSHFLQGAKKNNLSLALTLLEMTGDOREVSLGTSATNSVYTKKVENYVL 1499
    |||||
DB 1441 YRKKGVOESSHFLQGAKKNNLSLALTLLEMTGDOREVSLGTSATNSVYTKKVENYVL 1500
OY 1500 PKPDLPTSGKVELLPKHVIYQKDLFPTESNNGSPCHLDVGLSGLOTEGAIKMWENAR 1559
    |||||
DB 1501 PKPDLPTSGKVELLPKHVIYQKDLFPTESNNGSPCHLDVGLSGLOTEGAIKMWENAR 1560
OY 1560 PGKVPFLRATVETSSAKTSLDPLDPLANDNHYGQIPIKEKMSOEBSPKTAFFKKDITILS 1619
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DB 1561 PGKVPFLRATVETSSAKTSLDPLDPLANDNHYGQIPIKEKMSOEBSPKTAFFKKDITILS 1620
OY 1620 LNAESNHAIAAINGONKPEIEVTWAKOGRTERLCSQNPVLKRNOREITRTLLSDOE 1679
    |||||
DB 1621 LNAESNHAIAAINGONKPEIEVTWAKOGRTERLCSQNPVLKRNOREITRTLLSDOE 1680
OY 1680 EIDYDITISVEKKKDDPIYDEENOSPRFOKKTHTYIAVERLMDYMGSSSPHLNR 1739
    |||||
DB 1681 EIDYDITISVEKKKDDPIYDEENOSPRFOKKTHTYIAVERLMDYMGSSSPHLNR 1740
OY 1740 RAQSGSVPOFKKVFQEFTDGSFTQPIYRGELNEHLGLGPYIRAEVEDNIMTVFRNOAS 1799
    |||||
DB 1741 RAQSGSVPOFKKVFQEFTDGSFTQPIYRGELNEHLGLGPYIRAEVEDNIMTVFRNOAS 1800
OY 1800 RPYSEYSSLIYEEDOROGAEPKRNPFKPNETKYFMKVOHMAPTKDEPCKAMAYFSD 1859
    |||||
DB 1801 RPYSEYSSLIYEEDOROGAEPKRNPFKPNETKYFMKVOHMAPTKDEPCKAMAYFSD 1860
OY 1860 VDLEKDVHSGLIGPLVCHTNTLNPAGROVVOEFALEFTTIDETKSWYTEMENENCR 1919
    |||||
DB 1861 VDLEKDVHSGLIGPLVCHTNTLNPAGROVVOEFALEFTTIDETKSWYTEMENENCR 1920
OY 1920 APCNIOMEDPTPRENREHAIINGYIMDTLPGLVWADODIRMYLLSMGSNNINISIFSG 1979
    |||||
DB 1921 APCNIOMEDPTPRENREHAIINGYIMDTLPGLVWADODIRMYLLSMGSNNINISIFSG 1980
OY 1980 HFTVTRKKEEYKMALYNLYPGVFETVEMLDPSKAGIMRVECLIGEHLHAGNSTLFLVYSNK 2039
    |||||
DB 1981 HFTVTRKKEEYKMALYNLYPGVFETVEMLDPSKAGIMRVECLIGEHLHAGNSTLFLVYSNK 2040
OY 2040 COPPLGASGHIRDPQITASGOYGOMAPKLARLHYSISINASTKEPFSWIKVDLAPMI 2099
    |||||
DB 2041 COPPLGASGHIRDPQITASGOYGOMAPKLARLHYSISINASTKEPFSWIKVDLAPMI 2100
OY 2100 IHGIKTQAGARQFSSLYISQITIMSLDGKMWQTRNGSTGLMFFGNVDSSGIKANIF 2159
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DB 2101 IHGIKTQAGARQFSSLYISQITIMSLDGKMWQTRNGSTGLMFFGNVDSSGIKANIF 2160
OY 2160 NPPIIARYIRLHPHTHSIRSTLRMLMCGDLNCSNMPLGESKALISDAQITASSYFTNMF 2219

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DB 2161 NPPIIARYIRLHPHTHSIRSTLRMLMCGDLNCSNMPLGESKALISDAQITASSYFTNMF 2220
    |||||
OY 2220 ATWSPSKARLHLQGRSNAMRPOVNNPKEMLOVDFOFOTMKRYVTGTTQGVKSLTSMYKEF 2279
    |||||
DB 2221 ATWSPSKARLHLQGRSNAMRPOVNNPKEMLOVDFOFOTMKRYVTGTTQGVKSLTSMYKEF 2280
    |||||
OY 2280 LISSODGHQWTLFPONGKVVYVFOGNDSTPPVNSLDBPLLTRRLRIHPQSWYHOIALR 2339
    |||||
DB 2281 LISSODGHQWTLFPONGKVVYVFOGNDSTPPVNSLDBPLLTRRLRIHPQSWYHOIALR 2340
    |||||
OY 2340 MEVLGCEADQDLY 2351
    |||||
DB 2341 MEVLGCEADQDLY 2352
    |||||

RESULT 50
AAW11389
ID AAW11389 standard; Protein: 2352 AA.
XX
AC AAW11389;
XX
DF 18-NOV-1997 (first entry)
XX
DE Active Factor VIII:C analogue residue 563 P Insertion.
XX
KW Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW plasma protease; thrombin; immunogen; antibody; haemophilia; therapy;
KW proteolytic cleavage.
XX
OS Homo sapiens.
OS Synthetic.
XX
FH Key location/Qualifiers
FT /note= "signal peptide"
FT Protein 20..2352
FT /note= "mature Factor VIII:C"
FT Region 20..1668
FT /note= "heavy chain fragment"
FT Misc-difference 582
FT /note= "inserted residue"
FT Region 1669..2351
FT /note= "light chain fragment"
FT Domain 761..1668
FT /note= "B domain"
XX
XX MO9703195-A1.
XX
XX 30-JAN-1997.
XX
XX 09-JUL-1996; 96MO-US11444.
XX
XX 11-JUL-1995; 95US-0001025.
XX
XX (CHIR ) CHIRON CORP.
XX
XX Cohen FE, Hung DT, Innis M;
XX
XX WPI; 1997-119050/11.
XX
XX Factor VIII:C analog modified adjacent to a non-activating Arg
XX residue - used in the treatment of haemophilias, by improvement of
XX haemostasis
XX
XX Claim 21: Page -: 90pp; English.
XX
CC AAW11330-W11472 represent active Factor VIII:C analogues of the
CC invention. These sequences were created by mutating the wild type Factor
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC analogues comprise a native Factor VIII:C polypeptide modified at a site
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg

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CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophilias, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.

XX Sequence 2352 AA:

Query Match 99.9%; Score 12407.5; DB 18; Length 2352;

Best Local Similarity 100.0%; Pred. No. 0;

Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

OY 1 MOELSTCFELCLLRCSFATRRYYLGAVELSMQSDIGELPDARPPRVKSPFN 60  
DB 1 MOELSTCFELCLLRCSFATRRYYLGAVELSMQSDIGELPDARPPRVKSPFN 60  
OY 61 TSVYKKTLFEVETDHLFNIAKPPPMKGLLPTIOAEVDTVITLKMAHPVSLHAV 120  
DB 61 TSVYKKTLFEVETDHLFNIAKPPPMKGLLPTIOAEVDTVITLKMAHPVSLHAV 120  
OY 121 GVSYWKASGEAEYDDOTSOREKEDDKVPFGSHYYVQVLEKENGPMASDPLCTLYSLH 180  
DB 121 GVSYWKASGEAEYDDOTSOREKEDDKVPFGSHYYVQVLEKENGPMASDPLCTLYSLH 180  
OY 181 VDIKVDLSGLIGALLVCREGSLAKEKTOILHRTLLFNFEDGKSWHSEKNSLMQDRD 240  
DB 181 VDIKVDLSGLIGALLVCREGSLAKEKTOILHRTLLFNFEDGKSWHSEKNSLMQDRD 240  
OY 241 AASARAMPKMHYNGVYNSLPELIGCHRSYVWHVIGMGTPEVHSITFLEGHTFLVNH 300  
DB 241 AASARAMPKMHYNGVYNSLPELIGCHRSYVWHVIGMGTPEVHSITFLEGHTFLVNH 300  
OY 301 RQASBSRLTFLTAOTLLMDLGOFLFLCHSHSHQHDGMEAYVYVSCPEEQOLMKNE 360  
DB 301 RQASBSRLTFLTAOTLLMDLGOFLFLCHSHSHQHDGMEAYVYVSCPEEQOLMKNE 360  
OY 361 EAEDYDDDLTDSMDVVRDDDNSSPFOISVAKKHPTKWYIAAEEDMDAPLYLA 420  
DB 361 EAEDYDDDLTDSMDVVRDDDNSSPFOISVAKKHPTKWYIAAEEDMDAPLYLA 420  
OY 421 PDDRSYKSOYLNNGPORIGRKYKVFMAVYDDEFTKREAIQHESGILGPLLYGEVDTL 480  
DB 421 PDDRSYKSOYLNNGPORIGRKYKVFMAVYDDEFTKREAIQHESGILGPLLYGEVDTL 480  
OY 481 LIIIFKNOASRPYNYIPHGITDVRPLYSRRLPKGKHLKDPPLIPLGFIFFYKMTVVEGCP 540  
DB 481 LIIIFKNOASRPYNYIPHGITDVRPLYSRRLPKGKHLKDPPLIPLGFIFFYKMTVVEGCP 540  
OY 541 TKSDFRCLTRYSFVNMERDLASGLIGPLLICIKRESVDOR-GNQMISCKRNVILFESFD 599  
DB 541 TKSDFRCLTRYSFVNMERDLASGLIGPLLICIKRESVDOR-GNQMISCKRNVILFESFD 599  
OY 600 ENRSWYLTENIORFLNPAGVOLLEDPFOASINHSINGVYVFSQLSVCLAEVAYVYL 659  
DB 600 ENRSWYLTENIORFLNPAGVOLLEDPFOASINHSINGVYVFSQLSVCLAEVAYVYL 659  
OY 660 SIGAOTDFLSVFSGATYFKHKMYEDDTLTFPPSGETVPMSPMNPGLMILGCHNSDFPNR 719  
DB 660 SIGAOTDFLSVFSGATYFKHKMYEDDTLTFPPSGETVPMSPMNPGLMILGCHNSDFPNR 719  
OY 720 GMTALLKVSSCDKNTGDIYEDSTEDIISAYLLSKNNATPEPSQNSRHPSTRQOKFNAFT 779  
DB 720 GMTALLKVSSCDKNTGDIYEDSTEDIISAYLLSKNNATPEPSQNSRHPSTRQOKFNAFT 779  
OY 721 GHTALLKVSSCDKNTGDIYEDSTEDIISAYLLSKNNATPEPSQNSRHPSTRQOKFNAFT 780  
DB 721 GHTALLKVSSCDKNTGDIYEDSTEDIISAYLLSKNNATPEPSQNSRHPSTRQOKFNAFT 780

OY 780 IPENDIEKTPWFNAHRTPMKIQIONVSSDILLMLRQSPRHGSLSDLOEAKYETFSDDP 839  
DB 781 IPENDIEKTPWFNAHRTPMKIQIONVSSDILLMLRQSPRHGSLSDLOEAKYETFSDDP 840  
OY 840 SFGALDSNNSLSEMTNHRPQQLHNSGDWFTPEESDQLRLKEKIGTAAETELKIDFYVSS 899  
DB 841 SFGALDSNNSLSEMTNHRPQQLHNSGDWFTPEESDQLRLKEKIGTAAETELKIDFYVSS 900  
OY 900 TSNNLISITPISDNLAAGTNTSSILGPPMPVHYQSOLDITTLFGRKSSPLTESGCPILSE 959  
DB 901 TSNNLISITPISDNLAAGTNTSSILGPPMPVHYQSOLDITTLFGRKSSPLTESGCPILSE 960  
OY 960 ENNDKSLLESGLMNSQESSGKNVSTESGTLFRGRAGHPALLTMDNALPVSISLTKT 1019  
DB 961 ENNDKSLLESGLMNSQESSGKNVSTESGTLFRGRAGHPALLTMDNALPVSISLTKT 1020  
OY 1020 NKTNSNATNKRTHIDGPSLLIENSPPYWNILSDTEFKKVTPLIHDMIMDKNATALR 1079  
DB 1021 NKTNSNATNKRTHIDGPSLLIENSPPYWNILSDTEFKKVTPLIHDMIMDKNATALR 1080  
OY 1080 LHHMSNKTSSKNMENVQOKKEGPIPPDAQNPDKSFFKMLFLESARW1ORTHGKNSLNS 1139  
DB 1081 LHHMSNKTSSKNMENVQOKKEGPIPPDAQNPDKSFFKMLFLESARW1ORTHGKNSLNS 1140  
OY 1140 GGGSPKQVLSLGPESKSVBQNFLEKKKVVYVGGETTKVYGLKENVFPSSNPLFLNLD 1199  
DB 1141 GGGSPKQVLSLGPESKSVBQNFLEKKKVVYVGGETTKVYGLKENVFPSSNPLFLNLD 1200  
OY 1200 NLEHNNTHNDEKQLOEBIEIEKETLLIOENVVLPQIHTYTGTGRNPMKMLFLSTRONVEGSY 1259  
DB 1201 NLEHNNTHNDEKQLOEBIEIEKETLLIOENVVLPQIHTYTGTGRNPMKMLFLSTRONVEGSY 1260  
OY 1260 DGAIVAPVLDPRSLNSDNTNKTNHTAHFSKKGEBENLEGGNOTROYEKVACTRISPN 1319  
DB 1261 DGAIVAPVLDPRSLNSDNTNKTNHTAHFSKKGEBENLEGGNOTROYEKVACTRISPN 1320  
OY 1320 TSOQNFVTOBSKRALKQFLPLETELEKRIIYDPTSTQSKMKMLPSTLTQDIDNEYK 1379  
DB 1321 TSOQNFVTOBSKRALKQFLPLETELEKRIIYDPTSTQSKMKMLPSTLTQDIDNEYK 1380  
OY 1380 EKGATIOSPLSDCLTNRSHSIPQANSPLPIKAVSFPSPRIYTLTVFLPQDNSSHLPAAS 1439  
DB 1381 EKGATIOSPLSDCLTNRSHSIPQANSPLPIKAVSFPSPRIYTLTVFLPQDNSSHLPAAS 1440  
OY 1440 YKKDSGVQESSHFLQSAKKNNSLAILLLEMTGDRQREVGSLGTSATNSVTYKKYENTVL 1499  
DB 1441 YKKDSGVQESSHFLQSAKKNNSLAILLLEMTGDRQREVGSLGTSATNSVTYKKYENTVL 1500  
OY 1500 PKPDLPKTSGVELLIPKVHLYOKDLFPETSNKSPGHLDLVEGSLLOGTGEGAIKWEANR 1559  
DB 1501 PKPDLPKTSGVELLIPKVHLYOKDLFPETSNKSPGHLDLVEGSLLOGTGEGAIKWEANR 1560  
OY 1560 PGKVPFLKVAATESAKTPSKLDPLAMDHNHYGTOIPKPEEMKSOEKSPETAKKKDITLS 1619  
DB 1561 PGKVPFLKVAATESAKTPSKLDPLAMDHNHYGTOIPKPEEMKSOEKSPETAKKKDITLS 1620  
OY 1620 LNAESNNAIAINEGONKPELEYVMAOGFBERLCAONPVYLKRROREITETTLQSOOE 1679  
DB 1621 LNAESNNAIAINEGONKPELEYVMAOGFBERLCAONPVYLKRROREITETTLQSOOE 1680  
OY 1680 EIDYDQTSIVBKKREDDIYEDENQSPRSFOKTRHYFLAAVERLMDYGMSSSHVLARN 1739  
DB 1681 EIDYDQTSIVBKKREDDIYEDENQSPRSFOKTRHYFLAAVERLMDYGMSSSHVLARN 1740  
OY 1740 RAQSGVPOPKVYVFOEFTGSPFQPLVYGLJNEHLGLLPYRAEVEDNIWVTRNOAS 1799  
DB 1741 RAQSGVPOPKVYVFOEFTGSPFQPLVYGLJNEHLGLLPYRAEVEDNIWVTRNOAS 1800  
OY 1800 RPYSTYSSLISIEDDQOGAEPPKKNFVKNETKTYFKVQHHNAPTKDFDCKAAYFSD 1859  
DB 1801 RPYSTYSSLISIEDDQOGAEPPKKNFVKNETKTYFKVQHHNAPTKDFDCKAAYFSD 1860

QY 1860 VDLEKDVHSGGLIGPLVCHNTLNPAHGRVTVQEFALFTTIDETKSMYETENMERNCR 1919  
DB 1861 VDLEKDVHSGGLIGPLVCHNTLNPAHGRVTVQEFALFTTIDETKSMYETENMERNCR 1920  
QY 1920 APCNIOMEDPTFEKNEYRPHAINGYIMDTLPGLVMAODRIRMYLLSMGSNENHSHFSG 1979  
DB 1921 APCNIOMEDPTFEKNEYRPHAINGYIMDTLPGLVMAODRIRMYLLSMGSNENHSHFSG 1980  
QY 1980 HVEFTVARKKEEYKMAALYNYPGVETFEVEMLPKSKAGIMRVECLIGEHLAGHAGSTLFLVYSNK 2039  
DB 1981 HVEFTVARKKEEYKMAALYNYPGVETFEVEMLPKSKAGIMRVECLIGEHLAGHAGSTLFLVYSNK 2040  
QY 2040 COTPLGMAHGHRDQITRASQGYQONAPKRLAHYSGSINMSTKPEPSWIKYDILAPMI 2099  
DB 2041 COTPLGMAHGHRDQITRASQGYQONAPKRLAHYSGSINMSTKPEPSWIKYDILAPMI 2100  
QY 2100 IHGKTGARKOFSSLYISOFIIMYSIDGKKWQYRGNSTGTLAVFEGVNDSSGIRKHNIF 2159  
DB 2101 IHGKTGARKOFSSLYISOFIIMYSIDGKKWQYRGNSTGTLAVFEGVNDSSGIRKHNIF 2160  
QY 2160 NPPIIARVIRLPHPTYSIRSLRMEIMGCDLNSCSPMLGMEKATSDAQITRASSYFTNMF 2219  
DB 2161 NPPIIARVIRLPHPTYSIRSLRMEIMGCDLNSCSPMLGMEKATSDAQITRASSYFTNMF 2220  
QY 2220 ATWSPSKARLHLQGRSNAMRPQVNNPKEMLOVDFOKTKMKVTGVTQGVKSLTSMVYKEF 2279  
DB 2221 ATWSPSKARLHLQGRSNAMRPQVNNPKEMLOVDFOKTKMKVTGVTQGVKSLTSMVYKEF 2280  
QY 2280 LISSODGHOVTLFQNGKVVYVPOGNDSPFVAVNSLDPPLLTRLRIRHPQSWHQAIALR 2339  
DB 2281 LISSODGHOVTLFQNGKVVYVPOGNDSPFVAVNSLDPPLLTRLRIRHPQSWHQAIALR 2340  
QY 2340 MEVLGCEPADLY 2351  
DB 2341 MEVLGCEPADLY 2352

RESULT 51

AAM11394

ID AAM11394 standard; Protein; 2352 AA.

AC AAM11394;

DT 18-NOV-1997 (first entry)

DE Active Factor VIII:C analogue residue 561 F/E/P insertion.

XX Factor VIII:C analogue: glycoprotein; blood coagulation cascade;

KM fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;

KW plasma protease; thrombin; immunogen; antibody; haemophilia; therapy;

XX proteolytic cleavage.

OS Homo sapiens.

XX Synthetic.

FH Key Location/Qualifiers

FT Peptide 1..19

FT Protein /note= "signal peptide"

FT Region /note= "mature Factor VIII:C"

FT Modified-site /note= "heavy chain fragment"

FT Region /label= "Phe, Glu, Pro"

FT Domain /note= "inserted residue"

XX WO9703195-A1.

XX 30-JAN-1997.

XX 09-JUL-1996; 96MO-US11444.  
XX 11-JUL-1995; 95US-0001025.  
XX (CHIR ) CHIRON CORP.  
XX Cohen FE, Hung DT, Innis M;  
XX WPI; 1997-119050/11.  
XX Factor VIII:C analog modified adjacent to a non-activating Arg  
XX residue - used in the treatment of haemophilias, by improvement of  
XX haemostasis  
XX Claim 22: Page -, 90pp: English.  
XX AAM1130-W1472 represent active Factor VIII:C analogues of the  
XX invention. These sequences were created by mutating the wild type Factor  
XX VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
XX analogues comprise a native Factor VIII:C polypeptide modified at a site  
XX adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
XX dipeptide is created. Factor VIII:C is a large glycoprotein that  
XX participates in the blood coagulation cascade that ultimately converts  
XX soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
XX deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
XX X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is an  
XX activated by plasma proteases, such as thrombin. During activation the  
XX mature polypeptide is cleaved to generate heavy and light chain fragments  
XX that are further cleaved. Complexes of two or more of the analogues,  
XX nucleic acids and vectors encoding them may be used alone or in  
XX conjunction with each other, for the prevention or treatment of active  
XX Factor VIII:C deficiency in a mammal. The analogues may be used as  
XX immunogens to raise antibodies, and in the treatment of haemophilias, by  
XX improvement of haemostasis. The analogues are resistant to proteolytic  
XX cleavage and display increased plasma half-life. They may be administered  
XX at lower dosages and by different modes of administration.  
XX Sequence 2352 AA;

Query Match 99.9%; Score 12407.5; DB 18; Length 2352;

Best Local Similarity 100.0%; Pred. No. 0;

Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

QY 1 MOELSTCFPLCLRFQFSATRRYVIGAVELSDWMDSDGELPVDAKRPKPSFPN 60  
DB 1 MOELSTCFPLCLRFQFSATRRYVIGAVELSDWMDSDGELPVDAKRPKPSFPN 60  
QY 61 TSVYVKKTLFEVETDHLFHNIAKRPVPMGLGPTIOAEVYDTVITLKMAHPVSLAV 120  
DB 61 TSVYVKKTLFEVETDHLFHNIAKRPVPMGLGPTIOAEVYDTVITLKMAHPVSLAV 120  
QY 121 GVSYKASGAEYDDQISOREKEDDVFFGGSHYVYVQVLAENGPMSDPLCTYSYLSH 180  
DB 121 GVSYKASGAEYDDQISOREKEDDVFFGGSHYVYVQVLAENGPMSDPLCTYSYLSH 180  
QY 181 VDLYKDLNSGLIGALVLCREGSLAKKETQTLKFTILFAVEDEKSNHSTKNSLMQDRD 240  
DB 181 VDLYKDLNSGLIGALVLCREGSLAKKETQTLKFTILFAVEDEKSNHSTKNSLMQDRD 240  
QY 241 AASARWPKMHTVNGVYVRSIPGLIGCHRSYVYVNTOMGTPPVHSIFLEGTFVLRNH 300  
DB 241 AASARWPKMHTVNGVYVRSIPGLIGCHRSYVYVNTOMGTPPVHSIFLEGTFVLRNH 300  
QY 301 ROASLEISPTFLFQOTLMDLDFLCHISSHODMEAYVYVDSCPPEPOLRMKNNE 360  
DB 301 ROASLEISPTFLFQOTLMDLDFLCHISSHODMEAYVYVDSCPPEPOLRMKNNE 360  
QY 361 EADYVDDDLTSEMDVYVFPDDNSPSPFIOBSYAKKHPTVWHYIAAEEEDMYPALVLA 420  
DB 361 EADYVDDDLTSEMDVYVFPDDNSPSPFIOBSYAKKHPTVWHYIAAEEEDMYPALVLA 420  
QY 421 PDDRSYKSOYLNNGPORIGRKYKVRMAVDTETKTRBAIQHESGLIGPLLYGEGVDTL 480



Db	421	PDONSTYQOLINNGPQRIQKTKKRAFAAYIDELFKTIRELOHSESLIGLPLLYGEVDTL	480
Qy	481	LIFRKNQASRPNIYPHGJITDVRPLYSRRLPKGVKHLKDEPILLPEBIFKRYKWTYVEDGP	540
Db	481	LIFRKNQASRPNIYPHGJITDVRPLYSRRLPKGVKHLKDEPILLPEBIFKRYKWTYVEDGP	540
Qy	541	TKSDPRCLTRYSSPFNMNERDLASGLIGPILLICYKESVD -ORONQJMSQKRNVLTFVFD	599
Db	541	TKSDPRCLTRYSSPFNMNERDLASGLIGPILLICYKESVDORONQJMSQKRNVLTFVFD	600
Qy	600	EKRSMYLTENIOFRLPNRPAVOLEDPERQASINMHSINGYEDSIQOLSYCHAEVAWYIL	659
Db	601	EKRSMYLTENIOFRLPNRPAVOLEDPERQASINMHSINGYEDSIQOLSYCHAEVAWYIL	660
Qy	660	SIGACTDFLSVFEISGYTFKHKMYEDTLTFEPFSGETVEMSEMPGLWILGCHNSDERNR	719
Db	661	SIGACTDFLSVFEISGYTFKHKMYEDTLTFEPFSGETVEMSEMPGLWILGCHNSDERNR	720
Qy	720	GMTALLKXSSCDKNGDYEDSYEDISAYLLSKNNALTEPFSFQNSRHPSTROKOFNATT	779
Db	721	GMTALLKXSSCDKNGDYEDSYEDISAYLLSKNNALTEPFSFQNSRHPSTROKOFNATT	780
Qy	780	IPENDIEKTDPMWRAHRTPMKPTQNVSSDDLMLKROSPRPHGISLSDLOEAKYTEFSDP	839
Db	781	IPENDIEKTDPMWRAHRTPMKPTQNVSSDDLMLKROSPRPHGISLSDLOEAKYTEFSDP	840
Qy	840	SPGALDSNNLSLEKTHFRPOLHHSGDWYTFEPESGLQRLNEKGTTAATELKLDLFFVSS	899
Db	841	SPGALDSNNLSLEKTHFRPOLHHSGDWYTFEPESGLQRLNEKGTTAATELKLDLFFVSS	900
Qy	900	TENNLIISTIPBDNLAAGTDNTSSLGPPMPVHYOSOLDTLTEKXSSPLTESSGGPPLISE	959
Db	901	TENNLIISTIPBDNLAAGTDNTSSLGPPMPVHYOSOLDTLTEKXSSPLTESSGGPPLISE	960
Qy	960	ENNDKSLLESGLANSOESSMKNVSTSGRLFGRARHAPALLTKDNLKRVKSILKLT	1019
Db	961	ENNDKSLLESGLANSOESSMKNVSTSGRLFGRARHAPALLTKDNLKRVKSILKLT	1020
Qy	1020	NKTSNNSATNKTHIDGPSLLIENSPLYWQNILSDPEFKVPLIHDRLMDKNAALR	1079
Db	1021	NKTSNNSATNKTHIDGPSLLIENSPLYWQNILSDPEFKVPLIHDRLMDKNAALR	1080
Qy	1080	LHHSNKTTSSKNEMVQOKKEGPTIPROAPNDMSFPKMLFLPESARWIOPTHGKNSLNS	1139
Db	1081	LHHSNKTTSSKNEMVQOKKEGPTIPROAPNDMSFPKMLFLPESARWIOPTHGKNSLNS	1140
Qy	1140	GCGPSPKOLVSLGPEKSVBSONFLSEBKKVYVVGGEFTKDVGLKEWEPSSRNLFITND	1199
Db	1141	GCGPSPKOLVSLGPEKSVBSONFLSEBKKVYVVGGEFTKDVGLKEWEPSSRNLFITND	1200
Qy	1200	NHEHNNTNHOQKLOEIEIEKKEFTLQENVVV.PQIHTYTGKNNKMKMLFLISTROWEGSY	1259
Db	1201	NHEHNNTNHOQKLOEIEIEKKEFTLQENVVV.PQIHTYTGKNNKMKMLFLISTROWEGSY	1260
Qy	1260	DOAVAPVLODRSLNOSTNNTKTHAHSKSGEENLEGLGNOTKOIYVKACTTRISPN	1319
Db	1261	DOAVAPVLODRSLNOSTNNTKTHAHSKSGEENLEGLGNOTKOIYVKACTTRISPN	1320
Qy	1320	T5OQNFVYQSRKALKOFLPLEETELEKRIIVDTSTOMSKMKMLHPSTLTQIDYNEK	1379
Db	1321	T5OQNFVYQSRKALKOFLPLEETELEKRIIVDTSTOMSKMKMLHPSTLTQIDYNEK	1380
Qy	1380	EKGATTOPLSDCLTRHSHIPOANSRPLPIKVSFSPISPIYTLTVLVRPQDNSSHLPRAS	1439
Db	1381	EKGATTOPLSDCLTRHSHIPOANSRPLPIKVSFSPISPIYTLTVLVRPQDNSSHLPRAS	1440
Qy	1440	YKKRQSGVOESHTLOAKKNNLSLAILTEMTGDOREVSJGTSATNSYTYKKYENTVL	1499
Db	1441	YKKRQSGVOESHTLOAKKNNLSLAILTEMTGDOREVSJGTSATNSYTYKKYENTVL	1500
Qy	1500	PRPDLPRKTSQGVELLPRVAHYOKDLPEPETSNGSPGHLDVBSGLQEGEGAIKKNENNR	1559

Dd	1501	FKRDLPRKSKVVELLRKPHVLYQKRLPFTETLMSGNSGCHDLDLVESGLDQGBALIKNNENR	1560
Qy	1560	PGKVELPRVATTESSAKTDSKLLDLPLANDNHVGTQIQPKEMKSOEKSEPKTAFFKKTDTLLS	1619
Dd	1561	PGKVPFLRVATTESSAKTDSKLLDLPLANDNHVGTQIQPKEMKSOEKSEPKTAFFKKTDTLLS	1620
Qy	1620	LNACESNHAIAALINEGONKPRELEVYMAKQGTERRLCSONPVLAKRHQRELTFTTQLQSDOE	1679
Dd	1621	LNACESNHAIAALINEGONKPRELEVYMAKQGTERRLCSONPVLAKRHQRELTFTTQLQSDOE	1680
Qy	1680	EIVDDPDTISYEMKKEERPDIVDENQDSBPFOKTRNHYFAVRRLMDYGNSSPHVLRN	1739
Dd	1681	EIVDDPDTISYEMKKEERPDIVDENQDSBPFOKTRNHYFAVRRLMDYGNSSPHVLRN	1740
Qy	1740	RAQSGSVPOEKVKVVEQETDSSFTQPLRYKGLNELNHLGLGPRVIAEVEDNIWYTERNDAS	1799
Dd	1741	RAQSGSVPOEKVKVVEQETDSSFTQPLRYKGLNELNHLGLGPRVIAEVEDNIWYTERNDAS	1800
Qy	1800	RPYSFYSLSLYSEEDROGAERPKRFKPRMETKTFYFMVJOHNMAPTDEDFDCKAAAYTSD	1859
Dd	1801	RPYSFYSLSLYSEEDROGAERPKRFKPRMETKTFYFMVJOHNMAPTDEDFDCKAAAYTSD	1860
Qy	1860	VDLEKDVHSLGILRLLYCHTNTLMPARGROYMOERALTPTIDPEKSWYFTENNERCKR	1919
Dd	1861	VDLEKDVHSLGILRLLYCHTNTLMPARGROYMOERALTPTIDPEKSWYFTENNERCKR	1920
Qy	1920	APCNIOMEDPTFKENYRFHAINGYIMDTLPGLVMAODORIRMYLLMSGNSNENIHISHSFG	1979
Dd	1921	APCNIOMEDPTFKENYRFHAINGYIMDTLPGLVMAODORIRMYLLMSGNSNENIHISHSFG	1980
Qy	1980	HYFTVVRKKEEYKALYNLYPGVFEVEMLRSKAGIMRVBCILIGEHLHAGSTLFLVYSNK	2039
Dd	1981	HYFTVVRKKEEYKALYNLYPGVFEVEMLRSKAGIMRVBCILIGEHLHAGSTLFLVYSNK	2040
Qy	2040	CQTPYGMASGHIIDFOITASQYQGMAPKALRLHSGSINASTKEPFSYIKVDLAAPI	2099
Dd	2041	CQTPYGMASGHIIDFOITASQYQGMAPKALRLHSGSINASTKEPFSYIKVDLAAPI	2100
Qy	2100	IHGIKTQGAQKQKSSLYISQFIYMSLDGKKMOTYKGNSTGTLWVFFGYNDSGKIRHNIF	2159
Dd	2101	IHGIKTQGAQKQKSSLYISQFIYMSLDGKKMOTYKGNSTGTLWVFFGYNDSGKIRHNIF	2160
Qy	2160	NPIITARIKILATHTYNSITSTIRMBLWGCGLNCSMPAGMSKASISAOITASSYFTNMF	2219
Dd	2161	NPIITARIKILATHTYNSITSTIRMBLWGCGLNCSMPAGMSKASISAOITASSYFTNMF	2220
Qy	2220	ATWSPSKARLHLOGRSNANRPVNNPKEMQVDPQKTKVGTGTTQCVKSLTSMYKEF	2279
Dd	2221	ATWSPSKARLHLOGRSNANRPVNNPKEMQVDPQKTKVGTGTTQCVKSLTSMYKEF	2280
Qy	2280	LISSSQDGHOMTLFPGNGKVKVFKFGONDSFTPVVNSLDPRLTFRYLLIHPOSWVHQIALR	2339
Dd	2281	LISSSQDGHOMTLFPGNGKVKVFKFGONDSFTPVVNSLDPRLTFRYLLIHPOSWVHQIALR	2340
Qy	2340	MEVYGSCEAODLY 2351	
Dd	2341	MEVYGSCEAODLY 2352	
RESULT 52			
AAW11397			
ID AAW11397 standard; Protein: 2352 AA.			
AAW11397;			
Dd 18-NOV-1997 (first entry)			
XX Active Factor VIII:C analogue residue 747 p insertion.			
XX Factor VIII:C analogue; glycoprotein; blood coagulation cascade;			
KM fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;			
KM plasma protease; thrombin; immunogen; antibody; haemophilic therapy;			
KM proteolytic cleavage.			

XX Homo sapiens.  
OS Synthetic.  
XX Key Location/Qualifiers  
FH Peptide 1..19  
FT /note= "signal peptide"  
FT Protein 20..2352  
FT /note= "mature Factor VIII:C"  
FT Region 20..1668  
FT /note= "heavy chain fragment"  
FT Misc-difference 766  
FT /note= "inserted residue"  
FT Region 1669..2351  
FT /note= "light chain fragment"  
FT Domain 761..1668  
FT /note= "B domain"  
XX  
XX MO9703195-AI.  
XX  
XX 30-JAN-1997.  
XX  
XX 09-JUL-1996; 96WO-US11444.  
XX  
XX 11-JUL-1995; 95US-0001025.  
XX  
XX (CHIR ) CHIRON CORP.  
XX  
XX Cohen FE, Hung DT, Innis M;  
XX  
XX WPI: 1997-119050/11.  
XX  
XX Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophilia, by improvement of  
PT haemostasis  
XX  
XX Claim 23: Page -: 90pp; English.  
XX  
XX  
XX AAM11330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophilia, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX  
XX Sequence 2352 AA:  
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;  
QY 1 MOELSTCFLLRCFSATRRYLLGAVELSMYQSDGLPVDARPPVPRKSPFN 60  
DB 1 MOELSTCFLLRCFSATRRYLLGAVELSMYQSDGLPVDARPPVPRKSPFN 60  
QY 61 TSVYKKTLFEFTDLFNIAKRPVPMGLGPTIQAEVYDVVITLKNMASHPVSLHAY 120  
DB 61 TSVYKKTLFEFTDLFNIAKRPVPMGLGPTIQAEVYDVVITLKNMASHPVSLHAY 120

QY 121 GVSVMKASEGAEYDQTSQREKEDKVPFGSGSHYYVQVLKENGPMASDPICLITYSLSH 180  
DB 121 GVSVMKASEGAEYDQTSQREKEDKVPFGSGSHYYVQVLKENGPMASDPICLITYSLSH 180  
QY 181 VDLVYKDLNSGLIGALLVREGSLAKKEKQTLHKFILLFVPEDEKSMHSETKNSLMQDRD 240  
DB 181 VDLVYKDLNSGLIGALLVREGSLAKKEKQTLHKFILLFVPEDEKSMHSETKNSLMQDRD 240  
QY 241 AASARAMPKMHVNGVYNSLPGLIGCHRSVYWHYIGKTFPEVHSLFEGHFTVLRNH 300  
DB 241 AASARAMPKMHVNGVYNSLPGLIGCHRSVYWHYIGKTFPEVHSLFEGHFTVLRNH 300  
QY 301 ROASLETSPITFLTAOTILMDLGGPFLFCHSHSHQHGMEAYVYKVDSPREPOLRMNNE 360  
DB 301 ROASLETSPITFLTAOTILMDLGGPFLFCHSHSHQHGMEAYVYKVDSPREPOLRMNNE 360  
QY 361 EAEDYDDDLTDSMDVYVRDDNNSFQIQRSVAKKPKPKVWHYVIAAEEDMDVAPLVLA 420  
DB 361 EAEDYDDDLTDSMDVYVRDDNNSFQIQRSVAKKPKPKVWHYVIAAEEDMDVAPLVLA 420  
QY 421 PDDRSYSQYLNNGPQIRGKRYKRFMAAYDETFTKREAIQHESGILGPLYLGEVGDTL 480  
DB 421 PDDRSYSQYLNNGPQIRGKRYKRFMAAYDETFTKREAIQHESGILGPLYLGEVGDTL 480  
QY 481 LIIRKNOASRPYNTYRGITDVPRPLXSRRLKQVYKHDKDPILPGEIFYKMTVYEDGP 540  
DB 481 LIIRKNOASRPYNTYRGITDVPRPLXSRRLKQVYKHDKDPILPGEIFYKMTVYEDGP 540  
QY 541 TKSDPRCLTRYSSFFVNMERDLASGLIGPLILCYKESVDQRGNQIMSDRNVILFSVEDE 600  
DB 541 TKSDPRCLTRYSSFFVNMERDLASGLIGPLILCYKESVDQRGNQIMSDRNVILFSVEDE 600  
QY 601 NRSKLTPEINQRLPMPAGVQLEDEPFQASNMHSINGVFDLSQVCLHFAVAYWYLS 660  
DB 601 NRSKLTPEINQRLPMPAGVQLEDEPFQASNMHSINGVFDLSQVCLHFAVAYWYLS 660  
QY 661 IGAQDFLSVFFSGYTFKHKMYEDTLTLPFSGETVPMSENPGLMILGCHNSDFRRNG 720  
DB 661 IGAQDFLSVFFSGYTFKHKMYEDTLTLPFSGETVPMSENPGLMILGCHNSDFRRNG 720  
QY 721 MVALKAVSCCKNTGQYVEDSVEDISAYLSKNNAIIPRSPSONS-RHSPQKQFNATT 779  
DB 721 MVALKAVSCCKNTGQYVEDSVEDISAYLSKNNAIIPRSPSONS-RHSPQKQFNATT 779  
QY 781 IPENDIEKTDWFAHRTPMKIONVSSSDLMILKQSTPHGLISLDDQAEYTFSDP 840  
DB 781 IPENDIEKTDWFAHRTPMKIONVSSSDLMILKQSTPHGLISLDDQAEYTFSDP 840  
QY 840 SPGALDSNNSLSEMTHRPQLHHSQDMVTPESGLOTLNKLGTTAATELKKLDFKVS 899  
DB 840 SPGALDSNNSLSEMTHRPQLHHSQDMVTPESGLOTLNKLGTTAATELKKLDFKVS 899  
QY 900 TSNNTLSTIPEDNIAAOTDWTSLGPPSPVHYOSLDLTLFFGKSSPLTESGPFSLSE 959  
DB 900 TSNNTLSTIPEDNIAAOTDWTSLGPPSPVHYOSLDLTLFFGKSSPLTESGPFSLSE 959  
QY 960 ENNDSKLLSEGLMANSQSSWGKNVSTESGRLFKGRAHGPAITLKNALFKVYSLSLKT 1019  
DB 960 ENNDSKLLSEGLMANSQSSWGKNVSTESGRLFKGRAHGPAITLKNALFKVYSLSLKT 1019  
QY 1020 NKTSSNKSATNKRTHIDPILLIENSQVQNTLESDTPEFKVPPLIHDRMLDKNATLAR 1079  
DB 1020 NKTSSNKSATNKRTHIDPILLIENSQVQNTLESDTPEFKVPPLIHDRMLDKNATLAR 1079  
QY 1080 LNMMSKTTSSKNNEMVQOKKEGP1PPDAQNDMSFFKMLFLPESARW10RTHGKNSLNS 1139  
DB 1080 LNMMSKTTSSKNNEMVQOKKEGP1PPDAQNDMSFFKMLFLPESARW10RTHGKNSLNS 1139  
QY 1140 GQGPSPKQVLSLGPBKSVYEQNLFSSKNVYVVGKEPFDKGLKEMVFPSSRLPLTIND 1199  
DB 1140 GQGPSPKQVLSLGPBKSVYEQNLFSSKNVYVVGKEPFDKGLKEMVFPSSRLPLTIND 1199  
QY 1200 NLHENHTHNOEKKIOEIERKETL10ENYVLPQ1HTVTGTAKNPKNLLFLSTRQNVESY 1259  
DB 1200 NLHENHTHNOEKKIOEIERKETL10ENYVLPQ1HTVTGTAKNPKNLLFLSTRQNVESY 1259

Db	1201	NHHEHNTNHOEKKIJOEBIEKKEETLJQENNVLPDQIHTYTGKNEFKMLSTLRQNVGSI	1260
Qy	1260	DGAVAPVLQDFRSLNDSTNRTKHTAHFSKKGEENLELGNOTQOIVEKYACTTRISPN	1319
Db	1261	DCAVAPVLQDFRSLNDSTNRTKHTAHFSKKGEENLELGNOTQOIVEKYACTTRISPN	1320
Qy	1320	TSQQNFYVORSKRALKQFLRPLEETELEKRIYVDSTQSKMMKHLPTSTLQIDYNEK	1379
Db	1321	TSQQNFYVORSKRALKQFLRPLEETELEKRIYVDSTQSKMMKHLPTSTLQIDYNEK	1380
Qy	1380	EKGALTOSPRLSDCLTSHSHIQANSPRLPIAKVSSPSIRPIYLRVLVFONSSHLPAA5	1439
Db	1381	EKGALTOSPRLSDCLTSHSHIQANSPRLPIAKVSSPSIRPIYLRVLVFONSSHLPAA5	1440
Qy	1440	YAKKDSGVQESSHFLQAGAKNNLSLAILLEMTDQREVSGLSGTATNSVTYKRENTVL	1499
Db	1441	YAKKDSGVQESSHFLQAGAKNNLSLAILLEMTDQREVSGLSGTATNSVTYKRENTVL	1500
Qy	1500	PKPDLPRKSGVVELLPVHLYQKOLFPTETNSGSPGLDVEGSSLOGEGAKMNAKR	1559
Db	1501	PKPDLPRKSGVVELLPVHLYQKOLFPTETNSGSPGLDVEGSSLOGEGAKMNAKR	1560
Qy	1560	PKVFPFLVATTESSAKTPSKLLDPLAMDNIHGTOIPKEEKSOEKSPEKTAFAKKDPTIL5	1619
Db	1561	PKVFPFLVATTESSAKTPSKLLDPLAMDNIHGTOIPKEEKSOEKSPEKTAFAKKDPTIL5	1620
Qy	1620	LNACESNHAIAINEGONKPEIEVTMAKQRTKELCQONPPVLRKHOREITRTTLOSQOE	1679
Db	1621	LNACESNHAIAINEGONKPEIEVTMAKQRTKELCQONPPVLRKHOREITRTTLOSQOE	1680
Qy	1680	EIDYDQDTISVMKKEDDIDYDEENOSPSPFOKTRHYFAAVERLMQDGSSSPHYLRN	1739
Db	1681	EIDYDQDTISVMKKEDDIDYDEENOSPSPFOKTRHYFAAVERLMQDGSSSPHYLRN	1740
Qy	1740	RAOSSVQVQFKVYPOEFTDGSFTQPLYRGELNHELGLDLPYIRAEVEDNIMVTFRQAS	1799
Db	1741	RAOSSVQVQFKVYPOEFTDGSFTQPLYRGELNHELGLDLPYIRAEVEDNIMVTFRQAS	1800
Qy	1800	REYSFYSLSIYEEDQROGAEPKKNFVKNPTKTYFMKVYOHNAAPTCKDEFCOKAMAYFSD	1859
Db	1801	REYSFYSLSIYEEDQROGAEPKKNFVKNPTKTYFMKVYOHNAAPTCKDEFCOKAMAYFSD	1860
Qy	1860	VLEEDVHSGLIGPLVCHTNTLNPAHGROYVOEFLFTITDETKSYFENMERNCR	1919
Db	1861	VLEEDVHSGLIGPLVCHTNTLNPAHGROYVOEFLFTITDETKSYFENMERNCR	1920
Qy	1920	APCNTQMEDPFFKKNYFFHAINGYIMDTLPGIYMAOQRIRMVYLLSMGSNENIH5HPSG	1979
Db	1921	APCNTQMEDPFFKKNYFFHAINGYIMDTLPGIYMAOQRIRMVYLLSMGSNENIH5HPSG	1980
Qy	1980	HVFYTRKKEEKKALYMLYPGVFEVYEMLPKAGIMRVECLIGEHJHAAMSTLFLVYSNK	2039
Db	1981	HVFYTRKKEEKKALYMLYPGVFEVYEMLPKAGIMRVECLIGEHJHAAMSTLFLVYSNK	2040
Qy	2040	CQTPGLMASGHIRPOJTASGOYGOMAPRLARHYSSTIANWSTKRPFSWIKVLDLAPMI	2099
Db	2041	CQTPGLMASGHIRPOJTASGOYGOMAPRLARHYSSTIANWSTKRPFSWIKVLDLAPMI	2100
Qy	2100	HGIRTOGAROKFSSILYISQFIIMYSLDGKKMQTYRGNSTGTLMVFFGNVSSGKIHNF	2159
Db	2101	HGIRTOGAROKFSSILYISQFIIMYSLDGKKMQTYRGNSTGTLMVFFGNVSSGKIHNF	2160
Qy	2160	NPPIIARIRLPHPHYSIRSTLRMELMGCDLNSGSMPLGMSKSAISDAQITASSFTNMF	2219
Db	2161	NPPIIARIRLPHPHYSIRSTLRMELMGCDLNSGSMPLGMSKSAISDAQITASSFTNMF	2220
Qy	2220	ATWSSSKARLHLOGRSNAARPOVNNPKELVYDQKTMKYGTGTTQGVKSSLTSMYKEF	2279
Db	2221	ATWSSSKARLHLOGRSNAARPOVNNPKELVYDQKTMKYGTGTTQGVKSSLTSMYKEF	2280
Qy	2280	LIISSSDGHQWTLFFONGKVKVQGNQDSFTPVVNSLDPLLRVLRIRHPSQWVQIALR	2339

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Db	2465	MEVIGCEADPLY	2476
Qy	2465	MEVIGCEADPLY	2476
Db	2466	MEVIGCEADPLY	2477
Qy	2466		

conjunction with each other, for the prevention or treatment of active CC Factor VIII:C deficiency in a mammal. The analogues may be used as immunogens to raise antibodies, and in the treatment of hemophilias, by improvement of haemostasis. The analogues are resistant to proteolytic cleavage and display increased plasma half-life. They may be administered at lower dosages and by different modes of administration.

XX Sequence 2352 AA:

Query Match 99.98; Score 12407.5; DB 18; Length 2352;

Best Local Similarity 100.0%; Pred. No. 0; Mismatches 0; Indels 1; Gaps 1;

Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

QY 1 M0IELSTCFELCLLRFCSATRRYYLGAVELSWDMOSDLGELPYDARPPRYKSPFPN 60  
DB 1 M0IELSTCFELCLLRFCSATRRYYLGAVELSWDMOSDLGELPYDARPPRYKSPFPN 60  
QY 61 TSVYVKKTLFEFTDHLFNIAKRPMMGLGPTIOAEVDTVITLKNMASHPSLAHV 120  
DB 61 TSVYVKKTLFEFTDHLFNIAKRPMMGLGPTIOAEVDTVITLKNMASHPSLAHV 120  
QY 61 TSVYVKKTLFEFTDHLFNIAKRPMMGLGPTIOAEVDTVITLKNMASHPSLAHV 120  
DB 61 TSVYVKKTLFEFTDHLFNIAKRPMMGLGPTIOAEVDTVITLKNMASHPSLAHV 120  
QY 121 GVSYWKASEGAEYDQTSQREKEDKVPFGSHYVWQVINKENGPASDPLCLTYSYLSH 180  
DB 121 GVSYWKASEGAEYDQTSQREKEDKVPFGSHYVWQVINKENGPASDPLCLTYSYLSH 180  
QY 121 GVSYWKASEGAEYDQTSQREKEDKVPFGSHYVWQVINKENGPASDPLCLTYSYLSH 180  
DB 121 GVSYWKASEGAEYDQTSQREKEDKVPFGSHYVWQVINKENGPASDPLCLTYSYLSH 180  
QY 181 VDLVYKDLNSGLIGALLVCREGSLAKKETQTLKFTLLFAVFDEGKSWHSETKNSLMQDRD 240  
DB 181 VDLVYKDLNSGLIGALLVCREGSLAKKETQTLKFTLLFAVFDEGKSWHSETKNSLMQDRD 240  
QY 181 VDLVYKDLNSGLIGALLVCREGSLAKKETQTLKFTLLFAVFDEGKSWHSETKNSLMQDRD 240  
DB 181 VDLVYKDLNSGLIGALLVCREGSLAKKETQTLKFTLLFAVFDEGKSWHSETKNSLMQDRD 240  
QY 241 AASARAPKMHNTVNGYVNRSLPGLICGHRKSYVMYVIGMTTEPVHSIFLEGHTEFYVRNH 300  
DB 241 AASARAPKMHNTVNGYVNRSLPGLICGHRKSYVMYVIGMTTEPVHSIFLEGHTEFYVRNH 300  
QY 241 AASARAPKMHNTVNGYVNRSLPGLICGHRKSYVMYVIGMTTEPVHSIFLEGHTEFYVRNH 300  
DB 241 AASARAPKMHNTVNGYVNRSLPGLICGHRKSYVMYVIGMTTEPVHSIFLEGHTEFYVRNH 300  
QY 301 R0ASBELSPITELTAQTLMLMDLQGLFLFCHISSHODMEAYVAVVDSCPPEPOLRMKNNE 360  
DB 301 R0ASBELSPITELTAQTLMLMDLQGLFLFCHISSHODMEAYVAVVDSCPPEPOLRMKNNE 360  
QY 301 R0ASBELSPITELTAQTLMLMDLQGLFLFCHISSHODMEAYVAVVDSCPPEPOLRMKNNE 360  
DB 301 R0ASBELSPITELTAQTLMLMDLQGLFLFCHISSHODMEAYVAVVDSCPPEPOLRMKNNE 360  
QY 361 EAEDYDDDLTQSEMDVYRFDDNSPFTQIRSAKHKPTWVHYIAAEEEDMYAPLVYA 420  
DB 361 EAEDYDDDLTQSEMDVYRFDDNSPFTQIRSAKHKPTWVHYIAAEEEDMYAPLVYA 420  
QY 361 EAEDYDDDLTQSEMDVYRFDDNSPFTQIRSAKHKPTWVHYIAAEEEDMYAPLVYA 420  
DB 361 EAEDYDDDLTQSEMDVYRFDDNSPFTQIRSAKHKPTWVHYIAAEEEDMYAPLVYA 420  
QY 421 PDDRSYKSOYLNNGFQIRGRKYYKVRPMAYTDETEKTREATIOHESGILLGPLYGEVDTL 480  
DB 421 PDDRSYKSOYLNNGFQIRGRKYYKVRPMAYTDETEKTREATIOHESGILLGPLYGEVDTL 480  
QY 421 PDDRSYKSOYLNNGFQIRGRKYYKVRPMAYTDETEKTREATIOHESGILLGPLYGEVDTL 480  
DB 421 PDDRSYKSOYLNNGFQIRGRKYYKVRPMAYTDETEKTREATIOHESGILLGPLYGEVDTL 480  
QY 481 LLIFFKMOASRPVNIYPHGITDVRPLYSRRLPKGVKHLKDFPLIPGELFKKYKMYTVEDGP 540  
DB 481 LLIFFKMOASRPVNIYPHGITDVRPLYSRRLPKGVKHLKDFPLIPGELFKKYKMYTVEDGP 540  
QY 481 LLIFFKMOASRPVNIYPHGITDVRPLYSRRLPKGVKHLKDFPLIPGELFKKYKMYTVEDGP 540  
DB 481 LLIFFKMOASRPVNIYPHGITDVRPLYSRRLPKGVKHLKDFPLIPGELFKKYKMYTVEDGP 540  
QY 541 TKSDFPCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNOIMSDKRVNLLFSYFDE 600  
DB 541 TKSDFPCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNOIMSDKRVNLLFSYFDE 600  
QY 541 TKSDFPCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNOIMSDKRVNLLFSYFDE 600  
DB 541 TKSDFPCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNOIMSDKRVNLLFSYFDE 600  
QY 601 NRSWYLTENIOGFLPNPAGVOLEDEPEFOASINHSINGVVFQSLQVSCLENAVYVYIIS 660  
DB 601 NRSWYLTENIOGFLPNPAGVOLEDEPEFOASINHSINGVVFQSLQVSCLENAVYVYIIS 660  
QY 601 NRSWYLTENIOGFLPNPAGVOLEDEPEFOASINHSINGVVFQSLQVSCLENAVYVYIIS 660  
DB 601 NRSWYLTENIOGFLPNPAGVOLEDEPEFOASINHSINGVVFQSLQVSCLENAVYVYIIS 660  
QY 661 IGAQDTFLSVFFSGTYFKHKWYEDDTLTLPESGETFVPMSPNPGIATLGCNSDFFNRG 720  
DB 661 IGAQDTFLSVFFSGTYFKHKWYEDDTLTLPESGETFVPMSPNPGIATLGCNSDFFNRG 720  
QY 661 IGAQDTFLSVFFSGTYFKHKWYEDDTLTLPESGETFVPMSPNPGIATLGCNSDFFNRG 720  
DB 661 IGAQDTFLSVFFSGTYFKHKWYEDDTLTLPESGETFVPMSPNPGIATLGCNSDFFNRG 720  
QY 721 MTALIKVSSODKNTGDYEDSEYEDISAVILSKNNATIEPSSFQNSRPPSPRQOFNATLT 780  
DB 721 MTALIKVSSODKNTGDYEDSEYEDISAVILSKNNATIEPSSFQNSRPPSPRQOFNATLT 780  
QY 780 IPEMDIEKTDPMFAHRTMPKTIQNVSSDMLMLROSPTPHGLSISDQEAKEYTESDDP 839  
DB 780 IPEMDIEKTDPMFAHRTMPKTIQNVSSDMLMLROSPTPHGLSISDQEAKEYTESDDP 839  
QY 781 IPEMDIEKTDPMFAHRTMPKTIQNVSSDMLMLROSPTPHGLSISDQEAKEYTESDDP 840  
DB 781 IPEMDIEKTDPMFAHRTMPKTIQNVSSDMLMLROSPTPHGLSISDQEAKEYTESDDP 840  
QY 840 SPGAIDSNNSLSEMTFFRPOLHSGDWFTPEESGLQLRLNEKLGTTAATELKLDKFVSS 899  
DB 840 SPGAIDSNNSLSEMTFFRPOLHSGDWFTPEESGLQLRLNEKLGTTAATELKLDKFVSS 899  
QY 841 SPGAIDSNNSLSEMTFFRPOLHSGDWFTPEESGLQLRLNEKLGTTAATELKLDKFVSS 900  
DB 841 SPGAIDSNNSLSEMTFFRPOLHSGDWFTPEESGLQLRLNEKLGTTAATELKLDKFVSS 900

QY 900 TSNLSTIPSDNLACGTDNTSLGPPSMFVHYDSQDITLFGKSSPLTESGPIJLSSE 959  
DB 901 TSNLSTIPSDNLACGTDNTSLGPPSMFVHYDSQDITLFGKSSPLTESGPIJLSSE 960  
QY 960 ENNDKSLLESGLMNSQESSMGKNVSSPESRLEFKGRAGPALTLTKDALEFKYSISLTKT 1019  
DB 961 ENNDKSLLESGLMNSQESSMGKNVSSPESRLEFKGRAGPALTLTKDALEFKYSISLTKT 1020  
QY 1020 NKTSSNATNRKTHIDGSLIENSFSPWONILSDTEFFKVTPLIHDRMLDKNTAAR 1079  
DB 1021 NKTSSNATNRKTHIDGSLIENSFSPWONILSDTEFFKVTPLIHDRMLDKNTAAR 1080  
QY 1080 LNMHSKTTSSKNMVMQOKKEGPIPPDAONPMSPFKTLFPESARWIOETHGKNSLNS 1139  
DB 1081 LNMHSKTTSSKNMVMQOKKEGPIPPDAONPMSPFKTLFPESARWIOETHGKNSLNS 1140  
QY 1140 GGGSPKQVLSLQPEKSYVGONFLSEKNKYVKGFTYDQVLKEMVPPSSRNLFITNLD 1199  
DB 1141 GGGSPKQVLSLQPEKSYVGONFLSEKNKYVKGFTYDQVLKEMVPPSSRNLFITNLD 1200  
QY 1200 NLHNNTHNOEKKIOBEIEKKEETLIOENVVLPQIHVTGKNFMKNLFLSTRONVGSY 1259  
DB 1201 NLHNNTHNOEKKIOBEIEKKEETLIOENVVLPQIHVTGKNFMKNLFLSTRONVGSY 1260  
QY 1260 DGAYAPVLDQFNSLNDSTNRKTAHPSKKGEEENLEGINOTQIYEKACTTRISPN 1319  
DB 1261 DGAYAPVLDQFNSLNDSTNRKTAHPSKKGEEENLEGINOTQIYEKACTTRISPN 1320  
QY 1320 TSOQNEVYQSRKALQFRLPLEETELEKRIYDDTSTQMSKMKHLPPSTLQIDYNEK 1379  
DB 1321 TSOQNEVYQSRKALQFRLPLEETELEKRIYDDTSTQMSKMKHLPPSTLQIDYNEK 1380  
QY 1380 EKGATQSPISDCLTFSSHIPQANSPILAKVSPSIRPIYLRVLFQDNSSHLPAAS 1439  
DB 1381 EKGATQSPISDCLTFSSHIPQANSPILAKVSPSIRPIYLRVLFQDNSSHLPAAS 1440  
QY 1440 YRKDSGVQESSHFLQGAARKNNLSAIIITLMTGDOREVGSLGTSATNSYTYKKEVNTYL 1499  
DB 1441 YRKDSGVQESSHFLQGAARKNNLSAIIITLMTGDOREVGSLGTSATNSYTYKKEVNTYL 1500  
QY 1500 PKPLPPTSGKVELLKVHIIYOKDLPETNSGSPGLIDVEGSLLOGEGAIKWNENR 1559  
DB 1501 PKPLPPTSGKVELLKVHIIYOKDLPETNSGSPGLIDVEGSLLOGEGAIKWNENR 1560  
QY 1560 PKVYPLRVATESSAKTPSKLIDPLAMNHHGTQIPKEBKSOEKSEKPTAKKKDITLS 1619  
DB 1561 PKVYPLRVATESSAKTPSKLIDPLAMNHHGTQIPKEBKSOEKSEKPTAKKKDITLS 1620  
QY 1620 LMACSNHAIATINEGONKPELEVTMAQGRTERLCSQNPVYLKRHOREITRTTLQSDQE 1679  
DB 1621 LMACSNHAIATINEGONKPELEVTMAQGRTERLCSQNPVYLKRHOREITRTTLQSDQE 1680  
QY 1680 ETDYDDTISVEMKKEPDIYDEBENSQPSROKTRHVFYTAVERLMQVGMSSPHYLRN 1739  
DB 1681 ETDYDDTISVEMKKEPDIYDEBENSQPSROKTRHVFYTAVERLMQVGMSSPHYLRN 1740  
QY 1740 RAQSGSVQFQKVVQFQFTDGSFTQPLXRGELNHLGLGPLYRAEVDNIWTFRNQAS 1799  
DB 1741 RAQSGSVQFQKVVQFQFTDGSFTQPLXRGELNHLGLGPLYRAEVDNIWTFRNQAS 1800  
QY 1800 RPYSTYSSLIYEEDQOQAEPAKKNVVPNKETKYFMKVQVHHAPTKDEPDCKAANAYSFD 1859  
DB 1801 RPYSTYSSLIYEEDQOQAEPAKKNVVPNKETKYFMKVQVHHAPTKDEPDCKAANAYSFD 1860  
QY 1860 VDLERDVHSGLIGPLVLCNTNTLNPAGQVTVQFALFTTIDETKSWYFTBENRRCR 1919  
DB 1861 VDLERDVHSGLIGPLVLCNTNTLNPAGQVTVQFALFTTIDETKSWYFTBENRRCR 1920  
QY 1920 ACQNTQMDPFFKKNVFEHAINGYIMDTLPGLVMAQDRIKMYLLSGSNEHHSIHFSG 1979  
DB 1921 ACQNTQMDPFFKKNVFEHAINGYIMDTLPGLVMAQDRIKMYLLSGSNEHHSIHFSG 1980  
QY 1980 HVEFYRKKEEYKMALYNLPGEVTEVMLPSKAGIWRVECLIGEHLHAGNSTLFLYTSNK 2039

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|||||
Db      1981 HVFVTKREKYEKMAALYNYPGVETVEMLEPSKAGIRRVCECLIGELHAGNSTLELVYSNK 2040
      2040 CQPLGASGHI.RDQITASGOYGOMAPKLARLHSGSINAMSTKEPPSMYKDLAPMI 2099
      2041 CQPLGASGHI.RDQITASGOYGOMAPKLARLHSGSINAMSTKEPPSMYKDLAPMI 2100
Qy      2100 IHGKTQGAROKFSSLYISOFIIMYSIDGKKWQTVRGNSTGTLMVFGVNDSSGIRKHNIF 2159
      2101 IHGKTQGAROKFSSLYISOFIIMYSIDGKKWQTVRGNSTGTLMVFGVNDSSGIRKHNIF 2160
      2160 NPPIARIRLHPHTYSIRSTLRMELMGCDLNSCSWPLGMEKASIDQITASSYFTNMF 2219
      2161 NPPIARIRLHPHTYSIRSTLRMELMGCDLNSCSWPLGMEKASIDQITASSYFTNMF 2220
Qy      2220 ATWSPSKARLHLOGRNSMARPOVNNPKEMLOVDFOKTKMYGVYTGQYKSLTSMYVKEF 2279
      2221 ATWSPSKARLHLOGRNSMARPOVNNPKEMLOVDFOKTKMYGVYTGQYKSLTSMYVKEF 2280
Qy      2280 LISSQDGHQWTLFPQNGKRVKVEFGNODSFTPVVNSLDPELTFRYLRTHQSWVHQAIR 2339
      2281 LISSQDGHQWTLFPQNGKRVKVEFGNODSFTPVVNSLDPELTFRYLRTHQSWVHQAIR 2340
Qy      2340 MEVLGCEADLY 2351
      2341 MEVLGCEADLY 2352
Db

RESULT 54
AAW11374
ID      AAW11374 standard; Protein; 2352 AA.
AC      AAW11374;
XX      18-NOV-1997 (first entry)
XX      Active Factor VIII:C analogue residue 337 P insertion.
XX
KW      Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW      fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW      plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;
KW      proteolytic cleavage.
OS      Homo sapiens.
OS      Synthetic.
XX
FH      Key
FT      Peptide
FT      Protein
FT      Region
FT      Region
FT      Misc-difference
FT      Region
FT      Region
FT      Domain
XX      MO9703195-A1.
XX      30-JAN-1997.
XX      09-JUL-1996; 96MO-US11444.
XX      11-JUL-1995; 950S-0001025.
XX      (CHIR ) CHIRON CORP.
XX      Cohen FE, Hung DF, Innis M;
XX      PI
XX      WPI; 1997-119050/11.
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XX      Factor VIII:C analog modified adjacent to a non-activating Arg
PT      residue - used in the treatment of haemophilias, by improvement of
PT      haemostasis
XX      Claim 17; Page -: 90pp; English.
XX
CC      AAW11330-W1472 represent active Factor VIII:C analogues of the
CC      invention. These sequences were created by mutating the wild type Factor
CC      VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC      analogues comprise a native Factor VIII:C polypeptide modified at a site
CC      adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC      dipeptide is created. Factor VIII:C is a large glycoprotein that
CC      participates in the blood coagulation cascade that ultimately converts
CC      soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC      deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC      X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC      activated by plasma proteases, such as thrombin. During activation the
CC      mature polypeptide is cleaved to generate heavy and light chain fragments
CC      that are further cleaved. Complexes of two or more of the analogues,
CC      nucleic acids and vectors encoding them may be used alone or in
CC      conjunction with each other, for the prevention or treatment of active
CC      Factor VIII:C deficiency in a mammal. The analogues may be used as
CC      immunogens to raise antibodies, and in the treatment of haemophilias, by
CC      improvement of haemostasis. The analogues are resistant to proteolytic
CC      cleavage and display increased plasma half-life. They may be administered
CC      at lower dosages and by different modes of administration.
XX
SQ      Sequence 2352 AA:
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;
Best Local Similarity 100.0%; Pred. No. 0;
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;
Qy      1 MQELSTCFPLCLRFCEFSATRRYTLGAVELSDMYQSDLGELPYDAFRPPRPKSPFN 60
      1 MQELSTCFPLCLRFCEFSATRRYTLGAVELSDMYQSDLGELPYDAFRPPRPKSPFN 60
Db      1 TSVYVKKTLTFEFTDHLFNIAKPRPPMGLGPTIOAEYDTVTITLKNASHPVSLAHV 120
      61 TSVYVKKTLTFEFTDHLFNIAKPRPPMGLGPTIOAEYDTVTITLKNASHPVSLAHV 120
      61 TSVYVKKTLTFEFTDHLFNIAKPRPPMGLGPTIOAEYDTVTITLKNASHPVSLAHV 120
Qy      121 GVSYWKASEGAEYDDOTSOREKEDDKYFPGSGSHTYVWQVLEKENGPMASDPCLTYSYLSH 180
      121 GVSYWKASEGAEYDDOTSOREKEDDKYFPGSGSHTYVWQVLEKENGPMASDPCLTYSYLSH 180
      121 GVSYWKASEGAEYDDOTSOREKEDDKYFPGSGSHTYVWQVLEKENGPMASDPCLTYSYLSH 180
Db      121 VDIYKIDNSGLIGALINVBEGSLAKKERTOLHFFILLFVPEEGKSMHSEPKNSLMDQBD 240
      181 VDIYKIDNSGLIGALINVBEGSLAKKERTOLHFFILLFVPEEGKSMHSEPKNSLMDQBD 240
      181 VDIYKIDNSGLIGALINVBEGSLAKKERTOLHFFILLFVPEEGKSMHSEPKNSLMDQBD 240
Qy      241 AASARAPKMTYVNGVYVNSLPLGLICHRKSVYVHVGKTTPEVHSITLEGGTFLVRNH 300
      241 AASARAPKMTYVNGVYVNSLPLGLICHRKSVYVHVGKTTPEVHSITLEGGTFLVRNH 300
      241 AASARAPKMTYVNGVYVNSLPLGLICHRKSVYVHVGKTTPEVHSITLEGGTFLVRNH 300
Qy      301 ROASTLSPTTFLTAQTLMDLQGFLLFCHIISSHQHDGEAVYKVDSCPEPPOLR-MKNN 359
      301 ROASTLSPTTFLTAQTLMDLQGFLLFCHIISSHQHDGEAVYKVDSCPEPPOLR-MKNN 359
      301 ROASTLSPTTFLTAQTLMDLQGFLLFCHIISSHQHDGEAVYKVDSCPEPPOLR-MKNN 359
Db      301 ROASTLSPTTFLTAQTLMDLQGFLLFCHIISSHQHDGEAVYKVDSCPEPPOLR-MKNN 360
      360 BEARDYDDDLTSEMDYVRFPDDBNSPFIQIRSVAKKPKTWNHIAAEEDMDYAPLV 419
      361 BEARDYDDDLTSEMDYVRFPDDBNSPFIQIRSVAKKPKTWNHIAAEEDMDYAPLV 420
Qy      420 APDDRSTKSOYLNNGPQRTIGRKRYKVFPMAYTDEFTKREALQHSGLIGLVGXYGCT 479
      421 APDDRSTKSOYLNNGPQRTIGRKRYKVFPMAYTDEFTKREALQHSGLIGLVGXYGCT 480
      421 APDDRSTKSOYLNNGPQRTIGRKRYKVFPMAYTDEFTKREALQHSGLIGLVGXYGCT 480
Db      480 LLIIFFKNQASRPYNIYPHGIDVAPRLYSRRLPKGVKHLKDPFIIPLGETIFYKYKTYVVEDG 539
      481 LLIIFFKNQASRPYNIYPHGIDVAPRLYSRRLPKGVKHLKDPFIIPLGETIFYKYKTYVVEDG 540
      481 LLIIFFKNQASRPYNIYPHGIDVAPRLYSRRLPKGVKHLKDPFIIPLGETIFYKYKTYVVEDG 540
Qy      540 PTKSDPRCLTRYYSSPVNMEERDLASGLIGLLICYESVDQDGNQIMSDRNYLTVSVD 599
      541 PTKSDPRCLTRYYSSPVNMEERDLASGLIGLLICYESVDQDGNQIMSDRNYLTVSVD 600
      541 PTKSDPRCLTRYYSSPVNMEERDLASGLIGLLICYESVDQDGNQIMSDRNYLTVSVD 600
Db
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QY	600	ENRSMYLTENIORFLPNFAGVQLEDEPEFQASIMHSINGVYFSDLSQLSVCLHEAVAYTL	1659
DB	601	ENRSMYLTENIORFLPNFAGVQLEDEPEFQASIMHSINGVYFSDLSQLSVCLHEAVAYTL	1660
QY	660	SIGAOTDFLVSFSGYTPFKHKMYEDTFLTPFSGETVPMENRPMGLMTICGNSPFRK	719
DB	661	SIGAOTDFLVSFSGYTPFKHKMYEDTFLTPFSGETVPMENRPMGLMTICGNSPFRK	720
QY	720	GMTALLKVSCKKNTGDIYEDSTEDISAYLLSKNNAIPRPSFSONSRHSTROKOPNAT	779
DB	721	GMTALLKVSCKKNTGDIYEDSTEDISAYLLSKNNAIPRPSFSONSRHSTROKOPNAT	780
QY	780	IPENDIEKTDPMFAHRTMPMKIOWVSSDLMMLNQSPTPGHLSLSDQAKYETESDDP	839
DB	781	IPENDIEKTDPMFAHRTMPMKIOWVSSDLMMLNQSPTPGHLSLSDQAKYETESDDP	840
QY	840	SPGALDSNNSISEMTHFPOLHSGMDVFTPESGLQLRKNKLGTTAATLTKKLDPKYSS	899
DB	841	SPGALDSNNSISEMTHFPOLHSGMDVFTPESGLQLRKNKLGTTAATLTKKLDPKYSS	900
QY	900	TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHDSOLDTTLFGKSSPLTESGGLTISE	959
DB	901	TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHDSOLDTTLFGKSSPLTESGGLTISE	960
QY	960	ENNDKSLIESGLMNSQESMGKNVSTESGRLFKGRAGHAPALTKDNALFKYSISLKT	1019
DB	961	ENNDKSLIESGLMNSQESMGKNVSTESGRLFKGRAGHAPALTKDNALFKYSISLKT	1020
QY	1020	NKTSNNSATNRKTHIDGSLIENSPPVONITLEDTEFKVTLTIIDRMKKNATLR	1079
DB	1021	NKTSNNSATNRKTHIDGSLIENSPPVONITLEDTEFKVTLTIIDRMKKNATLR	1080
QY	1080	LNHMSKTTSSKNMVMVOOKKEGPIPPDQONPMSEFFMLFLPSASARIQRTGKXSLNS	1139
DB	1081	LNHMSKTTSSKNMVMVOOKKEGPIPPDQONPMSEFFMLFLPSASARIQRTGKXSLNS	1140
QY	1140	GOGPSPKOLVSLGPPEKSEVQONFLSEKKNVYVKGEBFTKDVGLKEMVFPSSRMLFTLND	1199
DB	1141	GOGPSPKOLVSLGPPEKSEVQONFLSEKKNVYVKGEBFTKDVGLKEMVFPSSRMLFTLND	1200
QY	1200	NLEHNTNHOEKKIOEIELEKETLIOENVYLPQIHVTGTSNEMKNLFLISTONWESGY	1259
DB	1201	NLEHNTNHOEKKIOEIELEKETLIOENVYLPQIHVTGTSNEMKNLFLISTONWESGY	1260
QY	1260	DGAYAPVLODFRSLNDSTNRKHTAHFSKGBEENLGLGNQTKQIYEKYACTTRISPN	1319
DB	1261	DGAYAPVLODFRSLNDSTNRKHTAHFSKGBEENLGLGNQTKQIYEKYACTTRISPN	1320
QY	1320	TSGOONFVOTORSKRALKOPRLPLEETLEKRIIVDDTSTOWSKNMKHLPTSLTQIDYNEK	1379
DB	1321	TSGOONFVOTORSKRALKOPRLPLEETLEKRIIVDDTSTOWSKNMKHLPTSLTQIDYNEK	1380
QY	1380	EKGATOSPLODCLTRHSITPOANRSPILPAVSSPSTIRPIYLRVLFDONSSHLPAS	1439
DB	1381	EKGATOSPLODCLTRHSITPOANRSPILPAVSSPSTIRPIYLRVLFDONSSHLPAS	1440
QY	1440	YRKKDSGVOESSHFLQAKKNNLSLAILTLEMTGDQREVSIGTSATNSVTYKKEVNTVL	1499
DB	1441	YRKKDSGVOESSHFLQAKKNNLSLAILTLEMTGDQREVSIGTSATNSVTYKKEVNTVL	1500
QY	1500	PKPDLPTSGKVELLPKHVYIQKDLPTETSNSSPGHLDIVESGLDGTGAKKMEAR	1559
DB	1501	PKPDLPTSGKVELLPKHVYIQKDLPTETSNSSPGHLDIVESGLDGTGAKKMEAR	1560
QY	1560	PGKVPFLRVATESSAKTPSKLDBPLAMDNHYGTQIPKCEMKSOEKSPKTAFFKKDITLS	1619
DB	1561	PGKVPFLRVATESSAKTPSKLDBPLAMDNHYGTQIPKCEMKSOEKSPKTAFFKKDITLS	1620
QY	1620	LNACESNHAAIAINGQKKPEIEVTMAKOGRTERLCSQNPVLRKHOREITRTTLQSDOE	1679
DB	1621	LNACESNHAAIAINGQKKPEIEVTMAKOGRTERLCSQNPVLRKHOREITRTTLQSDOE	1680

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QY	1680	EIDYDDTISVENKKEDEDDIYDEENOSPSPRSFOKTRHAYFLAVERLMDYGMSSSPHVLRN	1739
DB	1681	EIDYDDTISVENKKEDEDDIYDEENOSPSPRSFOKTRHAYFLAVERLMDYGMSSSPHVLRN	1740
QY	1740	RAOSSVPOFKKVVYFOEFTDGSFTQCLYGELENHILGILGYIAEVENIMVTRFNQAS	1799
DB	1741	RAOSSVPOFKKVVYFOEFTDGSFTQCLYGELENHILGILGYIAEVENIMVTRFNQAS	1800
QY	1800	RPTSFYSLSLISEEDQKGAEPKKNVKNKTKYFMKVYVHNAFPKDEFDOKAAYTSD	1859
DB	1801	RPTSFYSLSLISEEDQKGAEPKKNVKNKTKYFMKVYVHNAFPKDEFDOKAAYTSD	1860
QY	1860	VDEKDVHSGLIGPLVCHNTLNPAHQVTVQBFALFTTIDETKSWYFTENNERCR	1919
DB	1861	VDEKDVHSGLIGPLVCHNTLNPAHQVTVQBFALFTTIDETKSWYFTENNERCR	1920
QY	1920	APCNIQMEDPTFKENYRHAINGYINDTLPGLVMAQDORIRKWTLLSMGSNENHSHIRSG	1979
DB	1921	APCNIQMEDPTFKENYRHAINGYINDTLPGLVMAQDORIRKWTLLSMGSNENHSHIRSG	1980
QY	1980	HVFTYAKKEETKMAVLYNLYGVEEYVEMLPKSAKIMRYBCLIGEHLAGKSTLFLVYSNK	2039
DB	1981	HVFTYAKKEETKMAVLYNLYGVEEYVEMLPKSAKIMRYBCLIGEHLAGKSTLFLVYSNK	2040
QY	2040	CQPTLGMAISHIRDFQITASQYQGMAPKLARLHSGSINAMSTKEPFSWIVDILAPMI	2099
DB	2041	CQPTLGMAISHIRDFQITASQYQGMAPKLARLHSGSINAMSTKEPFSWIVDILAPMI	2100
QY	2100	IHGKTQGRKFSSKIVYSOFTIIMYSLDCKKKQYRGNSGTTLVFPFQVNDSSGIKHNF	2159
DB	2101	IHGKTQGRKFSSKIVYSOFTIIMYSLDCKKKQYRGNSGTTLVFPFQVNDSSGIKHNF	2160
QY	2160	NPTIARYLRLEPHYSIRSTLNLMEGLDNLSCMPJGMEKASISDAQTASSTFTYMF	2219
DB	2161	NPTIARYLRLEPHYSIRSTLNLMEGLDNLSCMPJGMEKASISDAQTASSTFTYMF	2220
QY	2220	ATWSPSKARLHLOGRSMANRPQVNNRKEWLVQDFQKTKKVTGVTQGVSKLTSMYKEE	2279
DB	2221	ATWSPSKARLHLOGRSMANRPQVNNRKEWLVQDFQKTKKVTGVTQGVSKLTSMYKEE	2280
QY	2280	LISSDQGHQWTLFPQNGKVKYFQGNODSFTVNVSLDPLPTRYLRHPOSMVQOILR	2339
DB	2281	LISSDQGHQWTLFPQNGKVKYFQGNODSFTVNVSLDPLPTRYLRHPOSMVQOILR	2340
QY	2340	MEVLGCEADOLY 2351	
DB	2341	MEVLGCEADOLY 2352	

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RESULT 55	
AAW1381	
ID AAW1381 standard; Protein: 2352 AA.	
XX	
AC AAW1381;	
XX	
DT 18-NOV-1997 (first entry)	
XX	
DE Active Factor VIII:C analogue residue 359 P insertion.	
XX	
KW Factor VIII:C: analogue; glycoprotein; blood coagulation cascade;	
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;	
KW plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;	
XX proteolytic cleavage.	
OS Homo sapiens.	
OS Synthetic.	
XX	
FT Key	Location/Qualifiers
FT Peptide	1..19
FT Protein	/note= "signal peptide"
FT	20..2352
FT	/note= "mature Factor VIII:C"
FT	20..1668
FT	Region

FT /note= "heavy chain fragment"  
FT Misc-difference 378  
FT Region /note= "inserted residue"  
FT 1669..2351  
FT /note= "light chain fragment"  
FT Domain 761..1668  
FT /note= "B domain"  
PN WO9703195-A1.  
PD 30-JAN-1997.  
XX 09-JUL-1996: 96MO-US11444.  
XX 11-JUL-1995: 95US-0001025.  
XX (CHIR ) CHIRON CORP.  
XX Cohen FE, Hung DT, Innis M;  
XX WPI: 1997-119050/11.  
XX  
XX Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophiliacs, by improvement of  
XX haemostasis  
XX  
XX Claim 19: Page -: 90pp; English.  
XX  
XX AAM1330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophiliacs, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX  
XX Sequence 2352 AA:  
SO  
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

Db 241 AASARAMPKMTVNGVYVRSIPGLICGHRKSYWVHWYIGMTTPEVHSTFLEGHTFLVRNH 300  
Qy 301 ROASISISPTFFLTAQTLMDLQGLFCHISSHQHDGMEAVKVDSCPEPOLRMKNE 360  
Db 301 ROASLEISPTFFLTAQTLMDLQGLFCHISSHQHDGMEAVKVDSCPEPOLRMKNE 360  
Qy 361 EADYDDDLTDEEMVY -RPDDDNPSFIOIRSVAKKHKMTVHWIHAEEEDMDYAPLV 419  
Db 361 EADYDDDLTDEEMVYAPREFDDNPSFIOIRSVAKKHKMTVHWIHAEEEDMDYAPLV 420  
Qy 420 APDRSYKQYVYNGNPGORIGKRYKRYFMAVYDFETFKREALQHESGILGLYGEVDT 479  
Db 421 APDRSYKQYVYNGNPGORIGKRYKRYFMAVYDFETFKREALQHESGILGLYGEVDT 480  
Qy 480 LLIIFKQASRPYNYTPGIDVAPLTSRLPRGVYHLKDPILPGEIFPKMTVYVEG 539  
Db 481 LLIIFKQASRPYNYTPGIDVAPLTSRLPRGVYHLKDPILPGEIFPKMTVYVEG 540  
Qy 540 PKSDPRLCTRYSSFFVNMEDLASGLIGPLICYKESYDQNGQIMSDKRNVLFSVD 599  
Db 541 PKSDPRLCTRYSSFFVNMEDLASGLIGPLICYKESYDQNGQIMSDKRNVLFSVD 600  
Qy 600 ENRSWLTENIQRFLLPNPAGVLEDPFOASNTMHSINGVYFDSIQSLCHEVAYWYL 659  
Db 601 ENRSWLTENIQRFLLPNPAGVLEDPFOASNTMHSINGVYFDSIQSLCHEVAYWYL 660  
Qy 660 STGAQTDLSVFFSGYTFKHKMYEDTLTFPPSGEYVMSNMENPGMLIGCHNSDFRNR 719  
Db 661 STGAQTDLSVFFSGYTFKHKMYEDTLTFPPSGEYVMSNMENPGMLIGCHNSDFRNR 720  
Qy 720 GMTALLKYSCKDKNTGVDEYSDVETSAVTLGSNNNAIEPRSPNSRHPSTROKONATT 779  
Db 721 GMTALLKYSCKDKNTGVDEYSDVETSAVTLGSNNNAIEPRSPNSRHPSTROKONATT 780  
Qy 780 IPENDIETDWFHARPPMKIOWVSSDLMLKQSPFGSLSDLOAKKETSDP 839  
Db 781 IPENDIETDWFHARPPMKIOWVSSDLMLKQSPFGSLSDLOAKKETSDP 840  
Qy 840 SPGAIDSNNSLSEMTHPRPOLHNSGDMVTPESGQLRLNKLGTATATLKLDFKVS 899  
Db 841 SPGAIDSNNSLSEMTHPRPOLHNSGDMVTPESGQLRLNKLGTATATLKLDFKVS 900  
Qy 900 TSNNTISTIPSDNLAAGDNTSSIGPSPMYHDSLODTTFGKSSPLRESGPISLSE 959  
Db 901 TSNNTISTIPSDNLAAGDNTSSIGPSPMYHDSLODTTFGKSSPLRESGPISLSE 960  
Qy 960 ENNDKLLBSGLMNSQSSWGNVSTESGRLFKGRRAHGALLTKDNLKVSISLKT 1019  
Db 961 ENNDKLLBSGLMNSQSSWGNVSTESGRLFKGRRAHGALLTKDNLKVSISLKT 1020  
Qy 1020 NKTSMNSATNKRTHIDGPSLLIENSPVQNTLJESDTEFKVPTLHIDRLMDKNATLR 1079  
Db 1021 NKTSMNSATNKRTHIDGPSLLIENSPVQNTLJESDTEFKVPTLHIDRLMDKNATLR 1080  
Qy 1080 LHMNSKNTSSKNNEMVQOKKEPTIPPDQNDPMSFFKMLFLPESARWIORHGKNSLNS 1139  
Db 1081 LHMNSKNTSSKNNEMVQOKKEPTIPPDQNDPMSFFKMLFLPESARWIORHGKNSLNS 1140  
Qy 1140 GGGSPKQVSLGPEKSEVQONFLSKNNVYVVGKEEFGKVDGLKEMVFPSSRNLFTLND 1199  
Db 1141 GGGSPKQVSLGPEKSEVQONFLSKNNVYVVGKEEFGKVDGLKEMVFPSSRNLFTLND 1200  
Qy 1200 NHEHNTNIOKKLOEIEIEKKFLLIOENNVLPQIHVTGKTFKKNLFLSTRONVESSY 1259  
Db 1201 NHEHNTNIOKKLOEIEIEKKFLLIOENNVLPQIHVTGKTFKKNLFLSTRONVESSY 1260  
Qy 1260 DGAVAPVLODFRSINDSTNRTKHTAHFSGKEEENLEGLONQKQIVKYYACTTSPN 1319  
Db 1261 DGAVAPVLODFRSINDSTNRTKHTAHFSGKEEENLEGLONQKQIVKYYACTTSPN 1320  
Qy 1320 TSQONFVYORSKRALKQFLPLEFTLEKRIYVDTSTQNSKNNKHLTSTLTQIDYNEK 1379  
Db 1321 TSQONFVYORSKRALKQFLPLEFTLEKRIYVDTSTQNSKNNKHLTSTLTQIDYNEK 1380



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QY 1380 EKGATGSPISDCLTRSHSIPQANRSPLEIAKVSSFPISIRPIYLTRVLFQDNSSHLPAAS 1439
DB 1381 EKGATGSPISDCLTRSHSIPQANRSPLEIAKVSSFPISIRPIYLTRVLFQDNSSHLPAAS 1440
QY 1440 YRKDSGVQESSHFLQAKAKNNISLAILLEMTGQREVGLSISATNNTYTKKYNTYL 1499
DB 1441 YRKDSGVQESSHFLQAKAKNNISLAILLEMTGQREVGLSISATNNTYTKKYNTYL 1500
QY 1500 PRPDLPTKSGVVELLPVNIYQKDLPEPTSGSGHDLVEGSLLOGTEGAIKMNEANR 1559
DB 1501 PRPDLPTKSGVVELLPVNIYQKDLPEPTSGSGHDLVEGSLLOGTEGAIKMNEANR 1560
QY 1560 PGKVPFLVATSSAKTPSKLDPLAMDNHGTQIPKEEMSOEKSEPKAFKKKDTILS 1619
DB 1561 PGKVPFLVATSSAKTPSKLDPLAMDNHGTQIPKEEMSOEKSEPKAFKKKDTILS 1620
QY 1620 LNACSNHAIANEGONKPEIEVTWAKQRTRELCSNPVLRHQREITRTTLOSDOE 1679
DB 1621 LNACSNHAIANEGONKPEIEVTWAKQRTRELCSNPVLRHQREITRTTLOSDOE 1680
QY 1680 EIDYDPTISVEKKEDPDYDEENOSPRSFKTRHYFIAVERLMDYGMSSSPHYLRN 1739
DB 1681 EIDYDPTISVEKKEDPDYDEENOSPRSFKTRHYFIAVERLMDYGMSSSPHYLRN 1740
QY 1740 RAQSGSVPOFKKVVPOEFTDGSFTOPLYRGELENEHLGILGPYIRAEVDNIMVTFRNQAS 1799
DB 1741 RAQSGSVPOFKKVVPOEFTDGSFTOPLYRGELENEHLGILGPYIRAEVDNIMVTFRNQAS 1800
QY 1800 RPYSFYSSLISYEEDORGAEPKRNKPYKPKETKTFMKYVOHMAPTDERDCKAMAYFSD 1859
DB 1801 RPYSFYSSLISYEEDORGAEPKRNKPYKPKETKTFMKYVOHMAPTDERDCKAMAYFSD 1860
QY 1860 VLEKDVHSGILGPLVCHNTLNPAGROYVYOEFALFTTIFDEITYSWTFTEMERNCR 1919
DB 1861 VLEKDVHSGILGPLVCHNTLNPAGROYVYOEFALFTTIFDEITYSWTFTEMERNCR 1920
QY 1920 APCNIQMEDPTEKEKYRFAHNGYIMDTLPGLYMADORIRMYLLSMGSMENIHSHIFSG 1979
DB 1921 APCNIQMEDPTEKEKYRFAHNGYIMDTLPGLYMADORIRMYLLSMGSMENIHSHIFSG 1980
QY 1980 HFTVYAKKEEKYKMALNYLPGVEFTEYBMLPSKAGITRREBCLIGELHLAGMSTLFVYSNK 2039
DB 1981 HFTVYAKKEEKYKMALNYLPGVEFTEYBMLPSKAGITRREBCLIGELHLAGMSTLFVYSNK 2040
QY 2040 CQTPILGMAHGHIRDFQITASGOYGOVMAKPLARLHSGSINAMSTKEPFSWIKYDLLAPMI 2099
DB 2041 CQTPILGMAHGHIRDFQITASGOYGOVMAKPLARLHSGSINAMSTKEPFSWIKYDLLAPMI 2100
QY 2100 IHGIKTQAGAROKFSSLYTSOFTIMYSLDGGKQWYRNGSTGIMVWFNGVNDSSGIXHNIF 2159
DB 2101 IHGIKTQAGAROKFSSLYTSOFTIMYSLDGGKQWYRNGSTGIMVWFNGVNDSSGIXHNIF 2160
QY 2160 NPPIIARYIRLHPHYISIRSLRMELMGCDLNSCSMPLESMESKALSDAQITASSYFTNNF 2219
DB 2161 NPPIIARYIRLHPHYISIRSLRMELMGCDLNSCSMPLESMESKALSDAQITASSYFTNNF 2220
QY 2220 ATWSPSKARLHLOGSNMARPVNNPKEWLOVDFOQTKMYGVGTTQGXSLLSMVKKE 2279
DB 2221 ATWSPSKARLHLOGSNMARPVNNPKEWLOVDFOQTKMYGVGTTQGXSLLSMVKKE 2280
QY 2280 LISSQDGHQWTLFPQNGKVVFVQGNDSFTPVVNSLDPRLTRYLRIHDSVWHQIALR 2339
DB 2281 LISSQDGHQWTLFPQNGKVVFVQGNDSFTPVVNSLDPRLTRYLRIHDSVWHQIALR 2340
QY 2340 MEVLGCEADOLY 2351
DB 2341 MEVLGCEADOLY 2352
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RESULT 56  
AAW11382  
ID AAW11382 standard; Protein; 2352 AA.

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XX AC AAW11382;
XX 18-NOV-1997 (first entry)
DT DT
XX DE Active Factor VIII:C analogue residue 360 P insertion.
XX KW Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
XX proteolytic cleavage.
OS Homo sapiens.
OS Synthetic.
PH Key
FT Location/Qualifiers
FT 1..19
FT /note= "signal peptide"
FT 20..2352
FT /note= "mature Factor VIII:C"
FT 20..1668
FT /note= "heavy chain fragment"
FT 379
FT /note= "inserted residue"
FT 1669..2351
FT /note= "light chain fragment"
FT 761..1668
FT /note= "B domain"
PN MO9703195-A1.
PD 30-JAN-1997.
XX 09-JUL-1996; 96NO-US11444.
XX 11-JUL-1995; 95US-0001025.
XX (CHIR ) CHIRON CORP.
PI Cohen FE, Hung DT, Innis M;
XX WPI; 1997-119050/11.
DR Factor VIII:C analog modified adjacent to a non-activating Arg
PT residue - used in the treatment of haemophiliacs, by improvement of
PT haemostasis
PS Claim 19; Page -: 90pp; English.
XX AAW11330-W1472 represent active Factor VIII:C analogues of the
CC invention. These sequences were created by mutating the wild type Factor
CC VIII:C coding sequence (see AAT5157) using mutagenic primers. The
CC analogues comprise a native Factor VIII:C polypeptide modified at a site
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC dipeptide is created. Factor VIII:C is a large glycoprotein that
CC participates in the blood coagulation cascade that ultimately converts
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC activated by plasma proteases, such as thrombin. During activation the
CC mature polypeptide is cleaved to generate heavy and light chain fragments
CC that are further cleaved. Complexes of two or more of the analogues,
CC nucleic acids and vectors encoding them may be used alone or in
CC conjunction with each other, for the prevention or treatment of active
CC Factor VIII:C deficiency in a mammal. The analogues may be used as
CC immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC improvement of haemostasis. The analogues are resistant to proteolytic
CC cleavage and display increased plasma half-life. They may be administered
CC at lower dosages and by different modes of administration.
XX Sequence 2352 AA:
SQ Query Match 99.9%; Score 12407.5; DB 18; Length 2352;
```



Best Local Similarity 100.0%: Pred. No. 0:					Matches 2351: Conservative 0: Mismatches 0: Indels 1: Gaps 1:				
QY	1	MOTELSTCEFFCLLPFCESATRRYYLGAVALSMDYQSDGLRYVDARPPRPKSPFN	60		QY	1080	LNMHNSKTTSSKMMVMQOKKEGPIPPDAONPMSPFKMLPLPSANWIRORTGKSLMS	1139	
Db	1	MOTELSTCEFFCLLPFCESATRRYYLGAVALSMDYQSDGLRYVDARPPRPKSPFN	60		Db	1081	LNMHNSKTTSSKMMVMQOKKEGPIPPDAONPMSPFKMLPLPSANWIRORTGKSLMS	1140	
QY	61	TSVYKKTLEFVETDHLFNIAKPRPMWGLGPTIOAEVYDVVYITLKNNASHPVSLAHV	120		QY	1140	GQGPSPKQVLSLGPESVGEONFLSEKNKVVVGGEFTKVGLKEMVPSSRLPLTJLND	1199	
Db	61	TSVYKKTLEFVETDHLFNIAKPRPMWGLGPTIOAEVYDVVYITLKNNASHPVSLAHV	120		Db	1141	GQGPSPKQVLSLGPESVGEONFLSEKNKVVVGGEFTKVGLKEMVPSSRLPLTJLND	1200	
QY	121	GVSYWKASGAEYDDOTSOREKEDDKVPGSGSTTYWQVILKENGPMSADPLCLTYSLSH	180		QY	1200	NLHEHNTNHOEKKIOEELIEKKEETLIOENNVLPQIHFTVGTGKFMKMLFLJLSTRQONEGSY	1259	
Db	121	GVSYWKASGAEYDDOTSOREKEDDKVPGSGSTTYWQVILKENGPMSADPLCLTYSLSH	180		Db	1201	NLHEHNTNHOEKKIOEELIEKKEETLIOENNVLPQIHFTVGTGKFMKMLFLJLSTRQONEGSY	1260	
QY	181	VDLYKDLNSGLIGALLVCREGSLAKEXTOTLHKFILLFAVDEBGSMSHSETKNSLMQDD	240		QY	1260	DGATAPVLDQFSLNDSNTNRKKTATFAFSKSGEENLBSLGNOTKOIYERKACTYRISPN	1319	
Db	181	VDLYKDLNSGLIGALLVCREGSLAKEXTOTLHKFILLFAVDEBGSMSHSETKNSLMQDD	240		Db	1261	DGATAPVLDQFSLNDSNTNRKKTATFAFSKSGEENLBSLGNOTKOIYERKACTYRISPN	1320	
QY	241	AASARAMPKMTVNGVYNRSLPGLIGCHRKSVMYVIGMGTTPEVHSIFLEGHTFLVRNH	300		QY	1320	TSQONFVOTRSKRALKQFRPLAEETLEKRIIVDDTSTQMSKNMKHLTPSTLQIDYNEK	1379	
Db	241	AASARAMPKMTVNGVYNRSLPGLIGCHRKSVMYVIGMGTTPEVHSIFLEGHTFLVRNH	300		Db	1321	TSQONFVOTRSKRALKQFRPLAEETLEKRIIVDDTSTQMSKNMKHLTPSTLQIDYNEK	1380	
QY	301	ROASLEISPTFLTQTLNDLGOFLFCHISSHOHGMEAVYKVDSCPEEPOLRKKNNE	360		QY	1380	EKGATQSPPLSDCLTRSHSTFOANRSPPLIAKVSFPSTIRPYTLRVLPQDNSSHLPAAS	1439	
Db	301	ROASLEISPTFLTQTLNDLGOFLFCHISSHOHGMEAVYKVDSCPEEPOLRKKNNE	360		Db	1381	EKGATQSPPLSDCLTRSHSTFOANRSPPLIAKVSFPSTIRPYTLRVLPQDNSSHLPAAS	1440	
QY	361	EADYDDDLTDSBMVVR-FDDNSPSFQIRSVAKRHKPTVWHYIAAEEEDMDVAPLVY	419		QY	1440	YRKDGSVOBSSHFTLOGAKKNNLSAILTLEMTGDOREVGLGTSATNSYTKKVENTYV	1499	
Db	361	EADYDDDLTDSBMVVR-FDDNSPSFQIRSVAKRHKPTVWHYIAAEEEDMDVAPLVY	419		Db	1441	YRKDGSVOBSSHFTLOGAKKNNLSAILTLEMTGDOREVGLGTSATNSYTKKVENTYV	1500	
QY	420	APDDRYSKYLNNGPORIGRKYKRVFMAVTEFEKTRREALIOHESGILGPLYGEGDY	479		QY	1500	PKPDLPTSGKVELLPKWHYIOKDLFPTETSNGPSGHDLVBSLLOGTBGAIKMNEANR	1559	
Db	421	APDDRYSKYLNNGPORIGRKYKRVFMAVTEFEKTRREALIOHESGILGPLYGEGDY	480		Db	1501	PKPDLPTSGKVELLPKWHYIOKDLFPTETSNGPSGHDLVBSLLOGTBGAIKMNEANR	1560	
QY	480	LIIFKKNQASRPYNIYPHGITDVRLYSRRLPGVYKHLKDPFLLIGEFKKYKTVYVEBG	539		QY	1560	PGKYPLFLVATESSAKTQSKLLDPLANDNHYGTQIRKEBKQOEKSPKTAFFKKOTIIS	1619	
Db	481	LIIFKKNQASRPYNIYPHGITDVRLYSRRLPGVYKHLKDPFLLIGEFKKYKTVYVEBG	540		Db	1561	PGKYPLFLVATESSAKTQSKLLDPLANDNHYGTQIRKEBKQOEKSPKTAFFKKOTIIS	1620	
QY	540	PTKSDPACLTRYYSSTVNNENDLASGLIGPLLCYKESVDORGNOJMSDKRNVILSVFD	599		QY	1620	LNCESNHAIAAINSONKPELIVYMAKOGTRRLCSQNPVYLAKHQREITRTTLDSDDE	1679	
Db	541	PTKSDPACLTRYYSSTVNNENDLASGLIGPLLCYKESVDORGNOJMSDKRNVILSVFD	600		Db	1621	LNCESNHAIAAINSONKPELIVYMAKOGTRRLCSQNPVYLAKHQREITRTTLDSDDE	1680	
QY	600	ENRSWYLTENIOFLPNPAGVOLDEPFOASNIMHSINGVYDLSQLSVCLHEVAWYIL	659		QY	1680	EIDYDPTIIVEMKKEDEFDIDEDENQSPRSFOKTRHYIAAVERLMDYGMSSSPHYLRN	1739	
Db	601	ENRSWYLTENIOFLPNPAGVOLDEPFOASNIMHSINGVYDLSQLSVCLHEVAWYIL	660		Db	1681	EIDYDPTIIVEMKKEDEFDIDEDENQSPRSFOKTRHYIAAVERLMDYGMSSSPHYLRN	1740	
QY	660	SIGANDPFLSVFSGYTPKHKWYEDPILTFPSSGETVPMSENGMLILGCHNSPFRNR	719		QY	1740	RAOGSVPQKKVYPOEFPDQSPQPLVYRGLMBNHLGLGPIYIRAEVEDNIMYTFRMOAS	1799	
Db	661	SIGANDPFLSVFSGYTPKHKWYEDPILTFPSSGETVPMSENGMLILGCHNSPFRNR	720		Db	1741	RAOGSVPQKKVYPOEFPDQSPQPLVYRGLMBNHLGLGPIYIRAEVEDNIMYTFRMOAS	1800	
QY	720	GMTALLKVSCKDKNMGDYEDSYEDISAYLLSKNNAIEPRSPSONSRHPSTRQOFNAT	779		QY	1800	RPSYFYSLSIYEBDOROGAERKRNKYKPNETKYTFWKVQHMAAPTQDEDFCKAMAFSD	1859	
Db	721	GMTALLKVSCKDKNMGDYEDSYEDISAYLLSKNNAIEPRSPSONSRHPSTRQOFNAT	780		Db	1801	RPSYFYSLSIYEBDOROGAERKRNKYKPNETKYTFWKVQHMAAPTQDEDFCKAMAFSD	1860	
QY	780	IPENDIEKTDPMFAHTRPMKIONVSSDDLMLLROSPTPHGLSTSDLOEKYTFESDPR	839		QY	1860	VDLEKDVHSGILGPLLVCHTNTLPNPAHGOVYTOEFAFLFTJFEDTKSMYTEMENRCR	1919	
Db	781	IPENDIEKTDPMFAHTRPMKIONVSSDDLMLLROSPTPHGLSTSDLOEKYTFESDPR	840		Db	1861	VDLEKDVHSGILGPLLVCHTNTLPNPAHGOVYTOEFAFLFTJFEDTKSMYTEMENRCR	1920	
QY	840	SPGAIDSNNSLSMTHFRPOLHSGDMVTFPESGLOLRINEKLGTTAATTELKIDFVSS	899		QY	1920	APCNIQMEDPTEKENRFAHNGYIMOTIGYVMAODOIRHYLLSMGSNNHISIHESG	1979	
Db	841	SPGAIDSNNSLSMTHFRPOLHSGDMVTFPESGLOLRINEKLGTTAATTELKIDFVSS	900		Db	1921	APCNIQMEDPTEKENRFAHNGYIMOTIGYVMAODOIRHYLLSMGSNNHISIHESG	1980	
QY	900	TSNNLISTIPSDMLAAGTDNNTSLGPPSPMVHYDSOLDJTLRGKSSPLTESGGPPLSLSE	959		QY	1980	HFTVRRKEEYKMAVLYNYPGVETVEMLDSKAGIMRVBCLIGEHLAAGNSTLEFLVYSNK	2039	
Db	901	TSNNLISTIPSDMLAAGTDNNTSLGPPSPMVHYDSOLDJTLRGKSSPLTESGGPPLSLSE	960		Db	1981	HFTVRRKEEYKMAVLYNYPGVETVEMLDSKAGIMRVBCLIGEHLAAGNSTLEFLVYSNK	2040	
QY	960	ENNDKSKLLESGLANSOESMGKNVSTPESGRLFKGRRAHGPALLKNDALKKVISTILTK	1019		QY	2040	COTPLGMAASHINDPITASGQYGMAPKLARLHYSGSIINAMSTKEPSSWIKVDLAPM1	2099	
Db	961	ENNDKSKLLESGLANSOESMGKNVSTPESGRLFKGRRAHGPALLKNDALKKVISTILTK	1020		Db	2041	COTPLGMAASHINDPITASGQYGMAPKLARLHYSGSIINAMSTKEPSSWIKVDLAPM1	2100	
QY	1020	NKTSNNSATNRKTHIDGPSLLIENSPSWONILLESOTERKKYTPLIHDMRLMDKNATALR	1079		QY	2100	IHGIRKTOGAQKQSSIXISQPIYHSLDDKKNQOTYGNSTGTLMPFPENDSSSIRKHNIF	2159	
Db	1021	NKTSNNSATNRKTHIDGPSLLIENSPSWONILLESOTERKKYTPLIHDMRLMDKNATALR	1080		Db	2101	IHGIRKTOGAQKQSSIXISQPIYHSLDDKKNQOTYGNSTGTLMPFPENDSSSIRKHNIF	2160	

QY 2160 NPPIIARYIRLHPHYSTRSLRMEIMGCDLNCSPMLCMEKASIDAOITASSYFTNNMF 2219  
DB 2161 NPPIIARYIRLHPHYSTRSLRMEIMGCDLNCSPMLCMEKASIDAOITASSYFTNNMF 2220  
QY 2220 ATWSPSKARLHLQGRSNMARPQVNNPKREMLQVDFORTKAVTGTQGVKSLTSMYKEF 2279  
DB 2221 ATWSPSKARLHLQGRSNMARPQVNNPKREMLQVDFORTKAVTGTQGVKSLTSMYKEF 2280  
QY 2280 LISSSDGHWMTLFPONGKVVYFQGNDSFTPVVNSLIDPILTRIRLRHPOSWHQAIALR 2339  
DB 2281 LISSSDGHWMTLFPONGKVVYFQGNDSFTPVVNSLIDPILTRIRLRHPOSWHQAIALR 2340  
QY 2340 MEVLGCEADPLY 2351  
DB 2341 MEVLGCEADPLY 2352

RESULT 57  
AAW11385  
ID AAW11385 standard; Protein: 2352 AA.  
XX  
AC AAW11385;  
DT 18-NOV-1997 (first entry)  
XX  
DE Active Factor VIII:C analogue residue 358 F/E/P insertion.  
XX  
KM Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;  
KM fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KM plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;  
XX proteolytic cleavage.  
OS Homo sapiens.  
OS Synthetic.  
FH Key Location/Qualifiers  
FT Peptide 1..19  
FT Protein /note= "signal peptide" 20..2352  
FT Region /note= "mature Factor VIII:C" 20..1668  
FT Modified-site /note= "heavy chain fragment" 377  
FT /label= Phe, Glu, Pro  
FT Region /note= "inserted residue" 1669..2351  
FT Domain /note= "light chain fragment" 761..1668  
FT /note= "B domain"

WO9703195-A1.  
XX  
PN 30-JAN-1997.  
XX  
PD 09-JUL-1996; 96WO-US11444.  
XX  
PE 11-JUL-1995; 95US-0001025.  
XX  
PA (CHIR ) CHIRON CORP.  
XX  
PI Cohen FE, Hung DT, Innis M;  
XX  
DR WPI; 1997-119050/11.  
XX  
PT Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophilias, by improvement of  
PT haemostasis  
XX  
XX Claim 20; Page -; 90pp; English.  
XX  
CC AAW1330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type factor

CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophilias, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX

SO Sequence 2352 AA.  
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;  
QY 1 MJETLSTCFELCLRFCHSATRRYYLGAVELSDWYMQSDLGELPVDARPPRPYKSPFN 60  
DB 1 MJETLSTCFELCLRFCHSATRRYYLGAVELSDWYMQSDLGELPVDARPPRPYKSPFN 60  
QY 61 TSVYVKKTLFVETTHLEFNIAKPPRPYGLPTAOAYVYVITLKNASHPVSLAHV 120  
DB 61 TSVYVKKTLFVETTHLEFNIAKPPRPYGLPTAOAYVYVITLKNASHPVSLAHV 120  
QY 121 GVSYWKASGAEYDQISQREKEDKVPFGSHYVWQVYLKENGPMASDPLCTTSYLSH 180  
DB 121 GVSYWKASGAEYDQISQREKEDKVPFGSHYVWQVYLKENGPMASDPLCTTSYLSH 180  
QY 121 GVSYWKASGAEYDQISQREKEDKVPFGSHYVWQVYLKENGPMASDPLCTTSYLSH 180  
DB 121 GVSYWKASGAEYDQISQREKEDKVPFGSHYVWQVYLKENGPMASDPLCTTSYLSH 180  
QY 181 VDLVKNLNSGLIGALLVCREGSLAKEKTYTLKFTLLFAVDECKSWHSETKNSLMODRD 240  
DB 181 VDLVKNLNSGLIGALLVCREGSLAKEKTYTLKFTLLFAVDECKSWHSETKNSLMODRD 240  
QY 241 AASARAPKMHVYVNGVYVRSIPGLIGCHRSYVYVHVGMTTPVSHIFLEGHTPLVRNH 300  
DB 241 AASARAPKMHVYVNGVYVRSIPGLIGCHRSYVYVHVGMTTPVSHIFLEGHTPLVRNH 300  
QY 301 ROASLEISPTFTTAQTLMDLQGFLLFCHISSHODMEAVYVVDSCPEEPOLRKNNE 360  
DB 301 ROASLEISPTFTTAQTLMDLQGFLLFCHISSHODMEAVYVVDSCPEEPOLRKNNE 360  
QY 361 EAEEDYDDDLTDEEMDV-VRFDDDSPEFTQIRSVAKKPKTWVHYIAAEEEDMDYAPLVL 419  
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DB 420 APDDRSTKQYIANNPQIRIGKTKKRYFMAAYVDEFKFKREAIQHESSITLPLLYGVDGT 479  
QY 480 LLIIFKNASRPYNIYPGILTDVAPLYSRRLPKGVKHLKDFPILPGEIFKYKTVYVEDG 539  
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DB 540 PTKSDPRCLTRYSSFFVNMERDLASGLIPLITCYKRESDVRGQIMSKRNVILFSEVD 599  
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DB 600 ENRSWYLTENIORFLPNPAGVQLEDEPQASIMHISNGYVFSLDLSVCLAHVAYWYL 659  
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DB 660 SIAQOTDLASFVFSGYTFKKMYVEDTLTLFFPSGSEYFVSMENPGIWLIGCHNSDFNR 719

QY 720 GMTALLKVSSCDKNTGDEYEDSYEDIISAYLLSKNNALIEPRSPFONSRRHPSTROKOFNAT 779  
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Db 721 GMTALLKVSSCDKNTGDEYEDSYEDIISAYLLSKNNALIEPRSPFONSRRHPSTROKOFNAT 780  
QY 780 IPENDIEKTDPMFAHHTPMFKIQNVSSDMLMLLROSPTPHGLSLSDQEAKEYTFESDDP 839  
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Db 901 TSNMLSTIPSDNLAAGTDNSTSLGPPSPMPVHDSOLDITLGGKSPSLTSGGSLSE 960  
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Db 1261 DGAYAPVLODFRSLNOSTNRKTHAHFSKSGEENLEGGNOTOYIEKACTRISPN 1320  
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Db 1381 EKAITQSPPLSDCLTRSHSIPQANRSPPLIAKVSFPISIRPIYLRVLFQDNSSHLPAAS 1440  
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Db 1621 LMACESNHATAINEONKPELEIETWMAOGTEBTLCSONPVYKXHOBEIRTLQSDOE 1680  
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Db 1681 EIDYDDTISVEKKEDFDIYDENQSPRSFOKKTRHYFLAAVERLMDYGMSSSPHYLRN 1740  
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Db 1741 RAOGSGVPOFKKVVFOEFTDGSFTQPLRGELNHLGLGPTIRAEVEDNIMVFRQAS 1800  
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Db 1801 RPIYSFYSLSIYEDDROGAEPRKKNFYVNPNETKITFYKVOHMAAPTKDEPDCAKAMATFSD 1860  
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Db 1861 VDLEKDVHSGSLIGPLLVCHTNTLNPANRGROYTQOERALEFTTFDETKSVYTEMENKNC 1920  
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Db 2281 LISSODGHOMTLFONGKVKVFOGNDSEFTPVVNSLDLPLRLRYLRJHPQSVHQAIALR 2340  
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Db 2341 MEVLGCEAODLY 2352  
|||||

RESULT 58  
AAW11388  
ID AAW11388 standard; Protein; 2352 AA.  
XX  
AC AAW11388;  
XX  
DT 18-NOV-1997 (first entry)  
XX  
DE Active Factor VIII:C analogue residue 562 P insertion.  
XX  
KW Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;  
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KW plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;  
KW proteolytic cleavage.  
OS Homo sapiens.  
OS Synthetic.  
XX  
FH key  
FT peptide  
FT 1..19 location/Qualifiers  
FT 20..2352 /note="signal peptide"  
FT Protein  
FT /note="mature Factor VIII:C"  
FT Region  
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FT Misc-difference  
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FT 1669..2351 /note-"light chain fragment"  
FT 761..1668 /note="B domain"  
XX  
FN MO9703195-A1.

XX 30-JAN-1997.  
PD 09-JUL-1996; 96WO-US11444.  
PF 11-JUL-1995; 95US-0001025.  
PR (CHIR ) CHIRON CORP.  
PA Cohen FE, Hung DT, Innis M;  
PI WPI, 1997-119050/11.  
XX Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophilias, by improvement of  
XX haemostasis  
PS Claim 21; Page -: 90pp; English.  
XX AA11330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophilias, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX  
SO Sequence 2352 AA:  
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;  
QY 1 MQIELSTCFELCLRFCEFSATRRYYLGAVELSDMYQSDGLGELPYDANFPPRYKSPFN 60  
DB 1 MQIELSTCFELCLRFCEFSATRRYYLGAVELSDMYQSDGLGELPYDANFPPRYKSPFN 60  
QY 61 TSVYKKTLFEFTDHLFRIAKPRPMWGLGPTIOAEYDVTVTLLKNMASHVSLHAV 120  
DB 61 TSVYKKTLFEFTDHLFRIAKPRPMWGLGPTIOAEYDVTVTLLKNMASHVSLHAV 120  
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DB 121 GSVYKASGAEAYDQTSREKEDDKYPPGSGHTYYWYVLAKNGMADPCLCTYSLSH 180  
QY 181 VDLVKDLSGLIGALVYREGSLAKETQTLNHFILLFAVPEDEKSMSETKNSLMQDD 240  
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QY 361 EADYDDDLTDSMDVVRPDONSPTQIRSAKKHPRKTWHYIAAEEDMDVAPLVLA 420  
DB 361 EADYDDDLTDSMDVVRPDONSPTQIRSAKKHPRKTWHYIAAEEDMDVAPLVLA 420

QY 421 PDDRKYKQVLANNGFORIGRKYKKVREMAVYDETETKRETAIONEHSGLIGLXGEVDTL 480  
DB 421 PDDRKYKQVLANNGFORIGRKYKKVREMAVYDETETKRETAIONEHSGLIGLXGEVDTL 480  
QY 481 LIIFKQASPNINYPHGITVYRPLYSRLPKYVXKHLDPFLGELFKKVVYVEDSP 540  
DB 481 LIIFKQASPNINYPHGITVYRPLYSRLPKYVXKHLDPFLGELFKKVVYVEDSP 540  
QY 541 TRSDPRLCTRYYSFVNMNERDLASGLIGPLLCYKESVDO- RGNQIMSDKRVNLYESVD 599  
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DB 720 GMTALTKVSSCDKNTGDIYEDSYEDISAYLLSKNNAIEPRFSQNSHHPSTROKONAT 779  
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DB 780 IPEMDIEKTDPMFAHRTMPKIQOVSSDLMLRQSPPHGLSLDQAKYETSDP 839  
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QY 1441 YRKKSQGVSESHFLQGAKKNNLFLALITLTEMGDQREVGSIGTSATNSYTYKKVENYV 1500  
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DB 1621 LNACSENHAIAMINEGONKPEIEVWAKGRTERTCSGNPVLKRHRREITRTTLOSDE 1680
QY 1680 EIDYDDTISVEMKEDDIYDEDENSPSPKTRHFTIAAVRLMDYMSSPVHLN 1739
DB 1681 EIDYDDTISVEMKEDDIYDEDENSPSPKTRHFTIAAVRLMDYMSSPVHLN 1740
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DB 1861 VDLEKDVHSGLIGPLVCHTNTLNPAGHQVVOEFALFTIPEETKSWTFENMERNCR 1920
QY 1920 APCNTQMEDPFEKKNYFHAINGYIMDTPLGLVMAQDRIWYILISGSMENHSHSESG 1979
DB 1921 APCNTQMEDPFEKKNYFHAINGYIMDTPLGLVMAQDRIWYILISGSMENHSHSESG 1980
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QY 2040 CQPLGMAHGHIRPOQTASGOYQWAPKLARLHSSGINSNWSKKEPFSIKVDLAPMI 2099
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DB 2101 HGKITGQAROKFSSLYISQFIIMYSIDSKKQWYRGNSTGLWVFGVNDSSGIRKHNIF 2160
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DB 2161 NPPIIARIYRIAPHYHSIRSTLMELMGCDLNSCNPJGMSKASIAQOITASSYTYNMF 2220
QY 2220 ATWSPSKARLHLQGRSNAMRPVNNPKEMLOYDFQKTKVYGVTTQGVKSILTSMTYKEF 2279
DB 2221 ATWSPSKARLHLQGRSNAMRPVNNPKEMLOYDFQKTKVYGVTTQGVKSILTSMTYKEF 2280
QY 2280 LISSSDGHHQMTLFFONGKVKVFOGNDSPFTPVNSLDPLLTTRYLRILHPOSWHQIALR 2339
DB 2281 LISSSDGHHQMTLFFONGKVKVFOGNDSPFTPVNSLDPLLTTRYLRILHPOSWHQIALR 2340
QY 2340 MEVLGCEAODLY 2351
DB 2341 MEVLGCEAODLY 2352

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RESULT 59  
AAM11357

ID AAM11357 standard; Protein: 2352 AA.

AC AAM11357;

DT 17-NOV-1997 (first entry)

DE Active Factor VIII:C analogue residue 278 F/E/P insertion.

XX Factor VIII:C analogue; glycoprotein; blood coagulation cascade;

KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;

```

KW plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;
KM proteolytic cleavage.
XX
OS Homo sapiens.
OS Synthetic.
XX
FH Key
FT 1..19 location/Qualifiers
FT /note="signal peptide"
FT 20..2352
FT /note="mature Factor VIII:C"
FT 20..1668
FT /note="heavy chain fragment"
FT 297
FT /label="Phe, Glu, Pro
FT /note="inserted residue"
FT 1669..2351
FT /note="light chain fragment"
FT 761..1668
FT /note="B domain"
XX
PN MO9703195-A1.
XX
PD 30-JAN-1997.
XX
PF 09-JUL-1996; 96MO-US11444.
XX
PR 11-JUL-1995; 95US-0001025.
XX
PA (CHIR ) CHIRON CORP.
XX
PI Cohen FE, Hung DT, Innis M;
DR WPI; 1997-119050/11.
XX
PT Factor VIII:C analog modified adjacent to a non-activating Arg
PT residue - used in the treatment of haemophilias, by improvement of
PT haemostasis
XX
PS Claim 14; Page -: 90pp; English.
XX
AAM11357-A1472 represent active Factor VIII:C analogues of the
CC invention. These sequences were created by mutating the wild type Factor
CC VIII:C coding sequence (see AAM11357) using mutagenic primers. The
CC analogues comprise a native Factor VIII:C polypeptide modified at a site
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC dipeptide is created. Factor VIII:C is a large glycoprotein that
CC participates in the blood coagulation cascade that ultimately converts
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC activated by plasma proteases, such as thrombin. During activation the
CC mature polypeptide is cleaved to generate heavy and light chain fragments
CC that are further cleaved. Complexes of two or more of the analogues,
CC nucleic acids and vectors encoding them may be used alone or in
CC conjunction with each other, for the prevention or treatment of active
CC Factor VIII:C deficiency in a mammal. The analogues may be used as
CC immunogens to raise antibodies, and in the treatment of haemophilias, by
CC improvement of haemostasis. The analogues are resistant to proteolytic
CC cleavage and display increased plasma half-life. They may be administered
CC at lower dosages and by different modes of administration.
XX
SQ Sequence 2352 AA;

```

Query Match 99.9%; Score 12407.5; DB 18; Length 2352;

Best Local Similarity 100.0%; Pred. No. 0;

Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

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QY 1 MOELSTCFPLCLLRCSFATRRYVIGAVELSMYMSDGLPVPARPPVPKSPFFN 60
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QY 61 TSVYKKTFLVEFTDHLFNAKRPMPMGLGPIQAEVYDVYVITLKNMASHPVSLHAV 120

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Db 61 TSVYKTLFEFTHLFIKAKPPPMGLGTLQAEYDVTYTLTKNNAHPVSHAV 120  
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Db 121 GVSVMKASGAEYDDOTSOREKEDDKVFGSGSHTYWQYLKENGPMASDPLCTLYSLH 180  
Qy 181 VDLVKDNLGGLGALLVCREGSLAKEKTQTLKFIILFAVDEGKSHSETKNSLMQDD 240  
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Db 241 AASARAMPKMTVNGYVRSLLPGLGCHRSYVMHIGMTTPEVHSIFLEGHFPL-VRN 299  
Qy 300 ~~HRASLTSPLTEFLAOTLMDLGOFLFCHLSSHQHGMEAYKVVDSCPEPOLMKKN~~ 359  
Db 301 ~~HRASLTSPLTEFLAOTLMDLGOFLFCHLSSHQHGMEAYKVVDSCPEPOLMKKN~~ 360  
Qy 360 EEAEDYDDDLJDEMDVYREDDDNSPFIQIRSVAKKHPTWVHYIAEEDMDYAPLV 419  
Db 361 EEAEDYDDDLJDEMDVYREDDDNSPFIQIRSVAKKHPTWVHYIAEEDMDYAPLV 420  
Qy 420 APDDRSYKSOYLNNGPORIGKXKXVRFMAJYDDEFTKREALIOHESGILPILYGEVGT 479  
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Qy 480 LLIIFKNQASRPYNTYPHGITDVRPLYSRRLPKGVKHLKDEPILPGEIFPKYKVTVEGD 539  
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Qy 780 IPENDIEKTDPMFAHRTPMKIQNVSSDLMMLRQSPTPHGLSLSDLOEAKYETPSDP 839  
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Qy 840 SPGALDSNNSLSEMTTHRRPOLHHSQMWTPPSSGLOLANKLGTATATLAKKLDKXSS 899  
Db 841 SPGALDSNNSLSEMTTHRRPOLHHSQMWTPPSSGLOLANKLGTATATLAKKLDKXSS 900  
Qy 900 TSNMLISTIPSDNLAAQTDNTSSIGPPSMRVHYDSQDLDTLFLGKSSPLESGLSLSE 959  
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Qy 960 ENNDSKLLSEGLMNSOSSWGNKVSSTESGRLEFKKRAHGALLTKNALFKVSIISLKT 1019  
Db 961 ENNDSKLLSEGLMNSOSSWGNKVSSTESGRLEFKKRAHGALLTKNALFKVSIISLKT 1020  
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Db 1201 NLHENNTHNOEKKIOEIEKKETLLQENNVVLPJHVTGTGKNRKNMLFLSLSTRONVBSY 1260  
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Db 1261 DGAYAPVLODFRSLNDSTNRKTHAHFSKKGEBENLEGLNQTOKOYEKYACTTRISP 1320  
Qy 1320 TSOONFYTORSKRALQOFLPLEETELEKRIYVDSTOWSKMKHLPPSTLTJODINEK 1379  
Db 1321 TSOONFYTORSKRALQOFLPLEETELEKRIYVDSTOWSKMKHLPPSTLTJODINEK 1380  
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Qy 1860 VDLKDVHSGLIGPFLVCHTNTLPNAGROYTVOERFLFETTFDETKSMYFTEMMERNCR 1919  
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|||||  
DB 2281 LISSQDGHQWTLFPGNKGKRVFGNODSFTPVNSLDLPRLFRYLRIHPQSWHQAIALR 2340  
QY 2340 MEVLGCEADQLY 2351  
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DB 2341 MEVLGCEADQLY 2352  
RESULT 60  
AAM1363  
ID AAM1363 standard: Protein, 2352 AA.  
XX  
AC AAM1363;  
XX  
DT 18-NOV-1997 (first entry)  
XX  
DE Active Factor VIII:C analogue residue 282 P insertion.  
XX  
KW Factor VIII:C analogue; glycoprotein; blood coagulation cascade;  
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KW plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;  
KW proteolytic cleavage.  
XX  
OS Homo sapiens.  
OS Synthetic.  
XX  
FH Key Location/Qualifiers  
FT Peptide 1..19  
FT /note= "signal peptide"  
FT Protein 20..2352  
FT /note= "mature Factor VIII:C"  
FT Region 20..1668  
FT /note= "heavy chain fragment"  
FT Misc-difference 301  
FT /note= "inserted residue"  
FT Region 1669..2351  
FT /note= "light chain fragment"  
FT Domain 761..1668  
FT /note= "B domain"  
XX  
XX MO9703195-A1.  
XX  
XX 30-JAN-1997.  
XX  
XX 09-JUL-1996; 96MO-US11444.  
XX  
XX 11-JUL-1995; 95US-0001025.  
XX  
XX (CHIR ) CHIRON CORP.  
XX  
XX Cohen FE, Hung DT, Innis M;  
XX  
XX MPI: 1997-119050/11.  
XX  
XX Factor VIII:C analog modified adjacent to a non-activating Arg  
XX residue - used in the treatment of haemophilias, by improvement of  
XX haemostasis  
XX  
XX Claim 15; Page -: 90pp; English.  
XX  
XX AAM1330-W11472 represent active Factor VIII:C analogues of the  
XX invention. These sequences were created by mutating the wild type Factor  
XX VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
XX analogues comprise a native Factor VIII:C polypeptide modified at a site  
XX adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
XX dipeptide is created. Factor VIII:C is a large glycoprotein that  
XX participates in the blood coagulation cascade that ultimately converts  
XX soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
XX deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
XX X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
XX activated by plasma proteases, such as thrombin. During activation the

CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophilias, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX  
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QY Query Match 99.9%; Score 12407.5; DB 18; Length 2352;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;  
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DB 361 EEAEDYDDDLTJSEMDVYRFDDNSPSFIOIRSVAKRHKPTVWHYIAEEDMDVAPLV 420  
QY 420 APDDRSTKSOYLNNGPORIGRKYKVFPMAYTEDEPKTEALIOHSSGILPILXGVSQGT 479  
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QY 480 LLIIFFKNQASRPYNIYPGIDVPRPLYSRRLPGVKNHLKDFPILPGELFYKKTVVEDEG 539  
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QY 660 SIGAQTDPLSVFEFSGYTFKHKVYEDTLTLPFGSETVMSMENGLMILGCHNSDFRN 719  
DB 661 SIGAQTDPLSVFEFSGYTFKHKVYEDTLTLPFGSETVMSMENGLMILGCHNSDFRN 720  
QY 720 GMTALKVSSCKNTGDDYEDSYEDISAYLSSNNNIEPRSSONSRRPSTROKONNAT 779  
DB 721 GMTALKVSSCKNTGDDYEDSYEDISAYLSSNNNIEPRSSONSRRPSTROKONNAT 780  
QY 780 IPEVDLEKTDPMFAHRTMPKTIQWVSSDMLMLRSPPHGLSLSDQEKKTETSDOP 839  
DB 781 IPEVDLEKTDPMFAHRTMPKTIQWVSSDMLMLRSPPHGLSLSDQEKKTETSDOP 840  
QY 840 SPGAIDSNNLSBMTNFRPOLHSGDMVFTPESGQLRLNEXKLTJTAATELKLDFKVS 899

|||||  
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|||||

Db 1921 APCNIQMEDPTFKENRFAHNGYIMDTLPGLVMAODQIRIMYILLMSGNENHSHIFSG 1980  
QY 1980 HPTVYRKKEEYKAMALYNLPYGVPEYVEMLPKAGIWRVECLIGEHLAGMSTFLYYSNK 2039  
Db 1981 HPTVYRKKEEYKAMALYNLPYGVPEYVEMLPKAGIWRVECLIGEHLAGMSTFLYYSNK 2040  
QY 2040 CQPLIMASGHIRDOFQIRASGOYQAMPKLARLHYSGSINAMSTKEPSWIKYDLAPMT 2099  
Db 2041 CQPLIMASGHIRDOFQIRASGOYQAMPKLARLHYSGSINAMSTKEPSWIKYDLAPMT 2100  
QY 2100 IHGKTQAGAROKFSSLYISOPTIWSLDGKKWQTYTNGNSTGTLMPFBNDDSGIKHNIF 2159  
Db 2101 IHGKTQAGAROKFSSLYISOPTIWSLDGKKWQTYTNGNSTGTLMPFBNDDSGIKHNIF 2160  
QY 2160 NPPIIARVIRLPHPTHYISIRSLRMEILGCDLNSCAMPLOMESKAISDAQIRASSYFTNMF 2219  
Db 2161 NPPIIARVIRLPHPTHYISIRSLRMEILGCDLNSCAMPLOMESKAISDAQIRASSYFTNMF 2220  
QY 2220 ATWSPSKARLHLQGRSNMARPQVNNPKEMIQVDFQTKMYGVGTTOGVKSILTSMYKEF 2279  
Db 2221 ATWSPSKARLHLQGRSNMARPQVNNPKEMIQVDFQTKMYGVGTTOGVKSILTSMYKEF 2280  
QY 2280 LISSQDGHQWTLFPONGKVKVYFQGNDSFTPVVNSLDPPLRLRYLRIRHPOSWVHQIALR 2339  
Db 2281 LISSQDGHQWTLFPONGKVKVYFQGNDSFTPVVNSLDPPLRLRYLRIRHPOSWVHQIALR 2340  
QY 2340 MEVLGCEADPLY 2351  
Db 2341 MEVLGCEADPLY 2352  
  
RESULT 61  
ID AAM11364  
X AC AAM11364; standard; protein; 2352 AA.  
X DT 18-NOV-1997 (first entry)  
X DE Active Factor VIII:C analogue residue 283 P insertion.  
X KW Factor VIII:C analogue; glycoprotein; blood coagulation cascade;  
X KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
X KW plasma protease; thrombin; immunogen; antibody; haemophilia; therapy;  
X KM proteolytic cleavage.  
X OS Homo sapiens.  
X OS Synthetic.  
X FH Key  
X FH Peptide  
X FT 1..19  
X FT /note="signal peptide"  
X FT 20..2352  
X FT /note="mature Factor VIII:C"  
X FT 20..1668  
X FT /note="heavy chain fragment"  
X FT 302  
X FT /note="inserted residue"  
X FT 1669..2351  
X FT /note="light chain fragment"  
X FT 761..1668  
X FT /note="B domain"  
X PN W09J03195-A1.  
X PD 30-JAN-1997.  
X PF 09-JUL-1996; 96WO-US11444.  
X PR 11-JUL-1995; 95US-0001025.  
X PA (CHIR ) CHIRON CORP.



PI Cohen FE, Hung DT, Innis M;  
XX MPI; 1997-119050/11.  
XX Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophiliacs, by improvement of  
PT haemostasis  
XX  
PS Claim 15; Page -: 90pp; English.  
XX  
CC AAM1330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see A451357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophiliacs, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX  
S0 Sequence 2352 AA;  
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

QY 540 PTKSDPRLCTIRYSSFVNMERDLASGLIGLLICVESYDQKQNOISDKRNILFESVD 599  
DB 541 PTKSDPRLCTIRYSSFVNMERDLASGLIGLLICVESYDQKQNOISDKRNILFESVD 600  
QY 600 ENRSWYLTENIQREFLPNAGVQLEDPEFOASINIMHINCINGVDSIQSLVCLHFAVWYTL 659  
DB 601 ENRSWYLTENIQREFLPNAGVQLEDPEFOASINIMHINCINGVDSIQSLVCLHFAVWYTL 660  
QY 660 SIGAQDTPLSVFSGTFRHKMYEDTLTLPESGFTVMSENGMLILGICNSDFRR 719  
DB 661 SIGAQDTPLSVFSGTFRHKMYEDTLTLPESGFTVMSENGMLILGICNSDFRR 720  
QY 720 GMTALLVSSCDKNTGDEYEDYEDISAVLLSKNNHIEPRFSQNSRHPSTROKQFNAT 779  
DB 721 GMTALLVSSCDKNTGDEYEDYEDISAVLLSKNNHIEPRFSQNSRHPSTROKQFNAT 780  
QY 780 IPENDIKTPMFAHRTMPKIQWVSSDDLMLRSPPHGLSLSDQEKAYEFSDP 839  
DB 781 IPENDIKTPMFAHRTMPKIQWVSSDDLMLRSPPHGLSLSDQEKAYEFSDP 840  
QY 840 SPGADISNNSLSMEHFRPOLHSGDVFPEESGLRLNEKLTGTTATETKLKDPKSS 899  
DB 841 SPGADISNNSLSMEHFRPOLHSGDVFPEESGLRLNEKLTGTTATETKLKDPKSS 900  
QY 900 TSNMLISTIPSDMLAGTDNTSSLGPPSMYVHDLSQDITLFGKSSPPLSEGSPLSE 959  
DB 901 TSNMLISTIPSDMLAGTDNTSSLGPPSMYVHDLSQDITLFGKSSPPLSEGSPLSE 960  
QY 960 ENDSKLLSEGLMNSQESSMCKNVSSTESGRLEFKGRRAHPALLTKDIALEKYSILRT 1019  
DB 961 ENDSKLLSEGLMNSQESSMCKNVSSTESGRLEFKGRRAHPALLTKDIALEKYSILRT 1020  
QY 1020 NKTSSNSATRKTHIDGPELILKNSPSWONILIESPTTEKKYTPPLIHDMILMKNKTAAR 1079  
DB 1021 NKTSSNSATRKTHIDGPELILKNSPSWONILIESPTTEKKYTPPLIHDMILMKNKTAAR 1080  
QY 1080 LNHHSKNTTSSKKNMEVQKKGEPLPPDAONPMKSFKNLFLPEASARIQRTGKKSLS 1139  
DB 1081 LNHHSKNTTSSKKNMEVQKKGEPLPPDAONPMKSFKNLFLPEASARIQRTGKKSLS 1140  
QY 1140 GQGPSKQVLSIGPEKSVBGONFLSEKKNVYVKGFTKQVGLKEMVPPSSRLPLTNLD 1199  
DB 1141 GQGPSKQVLSIGPEKSVBGONFLSEKKNVYVKGFTKQVGLKEMVPPSSRLPLTNLD 1200  
QY 1200 NLHENNTNHEKKTQIEIKKETTLLQENVVLPQIHVTGKKNFKMLNPLSTRONEGSV 1259  
DB 1201 NLHENNTNHEKKTQIEIKKETTLLQENVVLPQIHVTGKKNFKMLNPLSTRONEGSV 1260  
QY 1260 DGAYAPVLOPRLNDSTRTKTHAHPSKKGEEMLBELGNOTQIYEKACCTRTSPN 1319  
DB 1261 DGAYAPVLOPRLNDSTRTKTHAHPSKKGEEMLBELGNOTQIYEKACCTRTSPN 1320  
QY 1320 TSQONFYTQSKALKQFRLPLEETELEKRIYVDSTQWSKNMKHLPTSLTQIDYNEK 1379  
DB 1321 TSQONFYTQSKALKQFRLPLEETELEKRIYVDSTQWSKNMKHLPTSLTQIDYNEK 1380  
QY 1380 EKGAITQSPSLDCLTSHSIPQANSPRLPAKVSFSPRIPTYLTRVLFDONSSHLPAAS 1439  
DB 1381 EKGAITQSPSLDCLTSHSIPQANSPRLPAKVSFSPRIPTYLTRVLFDONSSHLPAAS 1440  
QY 1440 YRKKSQVOESSHFLOGAKKNLALITLLEMTGDDOREGSGTATSQVYKKEVENTVL 1499  
DB 1441 YRKKSQVOESSHFLOGAKKNLALITLLEMTGDDOREGSGTATSQVYKKEVENTVL 1500  
QY 1500 KRPLDPTSGVLELRLKXVHLYOKDLFPEFTSNGSPGHLDLVGSLLOCTBGAITKMEANR 1559  
DB 1501 KRPLDPTSGVLELRLKXVHLYOKDLFPEFTSNGSPGHLDLVGSLLOCTBGAITKMEANR 1560  
QY 1560 PKVPEFLRVATESSAATPSKLLDPLAMDNHGTQIPKEBMSQEKSPKTAFFKKKDTILS 1619  
DB 1561 PKVPEFLRVATESSAATPSKLLDPLAMDNHGTQIPKEBMSQEKSPKTAFFKKKDTILS 1620  
QY 1620 LMACSNHAIALINEGONKPEIEVTWAKOGBTERLCSQNPVLKRRHQREITRTTLODQE 1679

DB 1621 LNACESNHAIAIAINEQONKPEIEVWMAQGRTEKLSQNPVIAKBRQREIRRTLQSDQE 1680  
QY 1680 EIDYDDTISVEMKKEPDDIYDEDEQSPRSOKTTRHYFLAAVEMLMYGSSSPHLNR 1739  
DB 1681 EIDYDDTISVEMKKEPDDIYDEDEQSPRSOKTTRHYFLAAVEMLMYGSSSPHLNR 1740  
QY 1740 RAQSGVPOKRYVFOEFDDSGFTQPLRGSLNEHGLGPIYRAVEDNIMVTFNRQAS 1799  
DB 1741 RAQSGVPOKRYVFOEFDDSGFTQPLRGSLNEHGLGPIYRAVEDNIMVTFNRQAS 1800  
QY 1800 RPYSTYSSLSIYEEDQROGAEPKRNKVPYKNTKTYFMKVOHMAFPTKDEPCKAMAFSD 1859  
DB 1801 RPYSTYSSLSIYEEDQROGAEPKRNKVPYKNTKTYFMKVOHMAFPTKDEPCKAMAFSD 1860  
QY 1860 VLEKDVHSGILGPLLVCHTNFLNPAHGRQVTVQEFALFTTIEDTKSMYTFEMERNCR 1919  
DB 1861 VLEKDVHSGILGPLLVCHTNFLNPAHGRQVTVQEFALFTTIEDTKSMYTFEMERNCR 1920  
QY 1920 APCNIQMEDPTFKENRPHAINGYIMDTLPGLVADODQIRMYLLSMGSNENHSHIFSG 1979  
DB 1921 APCNIQMEDPTFKENRPHAINGYIMDTLPGLVADODQIRMYLLSMGSNENHSHIFSG 1980  
QY 1980 HFTYVRKKEEYKMAALNLYPGVETVEMLPKAGINRVECLIGEBLHAGMSTLEFLVYSNK 2039  
DB 1981 HFTYVRKKEEYKMAALNLYPGVETVEMLPKAGINRVECLIGEBLHAGMSTLEFLVYSNK 2040  
QY 2040 COTPLGMAHGHINDFOITASGOYGOMAPKLARLHYSGSINAMSTKEPSPWIKVDLAPMT 2099  
DB 2041 COTPLGMAHGHINDFOITASGOYGOMAPKLARLHYSGSINAMSTKEPSPWIKVDLAPMT 2100  
QY 2100 IHGKTQGAOKFSSLYISQFTIMTSLDGKKWOTYKGNSTGLMFPFNVDSSIKHNF 2159  
DB 2101 IHGKTQGAOKFSSLYISQFTIMTSLDGKKWOTYKGNSTGLMFPFNVDSSIKHNF 2160  
QY 2160 NPIIARIYRLHPHTSIRSTLRLMELMCDLNSCSPMLMESKASISDQITASSYFTNMF 2219  
DB 2161 NPIIARIYRLHPHTSIRSTLRLMELMCDLNSCSPMLMESKASISDQITASSYFTNMF 2220  
QY 2220 ATWSPKARLHLOGRANRPQVNNPKEMLOVDFOKTMKVTVGTTOGVKSLTSMYKFR 2279  
DB 2221 ATWSPKARLHLOGRANRPQVNNPKEMLOVDFOKTMKVTVGTTOGVKSLTSMYKFR 2280  
QY 2280 ITSSQDGHOWTLFPQNGKRVKVGONOSFPVYVNSLIDPLRLTRYLRIHQSWVHOIAR 2339  
DB 2281 ITSSQDGHOWTLFPQNGKRVKVGONOSFPVYVNSLIDPLRLTRYLRIHQSWVHOIAR 2340  
QY 2340 MEVLGCEKADLY 2351  
DB 2341 MEVLGCEKADLY 2352

RESULT 62  
AAW11368  
ID AAW11368 standard; Protein; 2352 AA.  
AC AAW11368;  
XX  
DT 18-NOV-1997 (first entry)  
XX  
DE Active Factor VIII:C analogue residue 281 F/E/P insertion.  
XX  
KW Factor VIII:C analogue; glycoprotein; blood coagulation cascade;  
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KW plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;  
KW proteolytic cleavage.  
XX  
OS Homo sapiens.  
OS Synthetic.  
XX  
FH Key  
FT Peptide 1..19 Location/Qualifiers  
FT /note= "signal peptide"

FT Protein 20..2352  
FT /note= "mature Factor VIII:C"  
FT Region 20..1668  
FT /note= "heavy chain fragment"  
FT Modified-site 300  
FT /label= "phe, glu, pro  
FT Region 1669..2351  
FT /note= "inserted residue"  
FT Domain 761..1668  
FT /note= "B domain"  
PN W09703195-A1.  
PD 30-JAN-1997.  
PD 09-JUL-1996; 96WO-US11444.  
PE 11-JUL-1995; 95US-0001025.  
PR (CHIR ) CHIRON CORP.  
PA Cohen FE, Hung DT, Innis M;  
PI WPI, 1997-119050/11.  
DR Factor VIII:C analog modified adjacent to a non-activating Arg  
XX residue - used in the treatment of haemophilias, by improvement of  
XX haemostasis  
PT Claim 16: Page -: 90pp; English.  
PS AAW11330-W1472 represent active Factor VIII:C analogues of the  
XX invention. These sequences were created by mutating the wild type Factor  
XX VIII:C coding sequence (see AY51357) using mutagenic primers. The  
XX analogues comprise a native Factor VIII:C polypeptide modified at a site  
XX adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
XX dipeptide is created. Factor VIII:C is a large glycoprotein that  
XX participates in the blood coagulation cascade that ultimately converts  
XX soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
XX deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
XX X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
XX activated by plasma proteases, such as thrombin. During activation the  
XX mature polypeptide is cleaved to generate heavy and light chain fragments  
XX that are further cleaved. Complexes of two or more of the analogues,  
XX nucleic acids and vectors encoding them may be used alone or in  
XX conjunction with each other, for the prevention or treatment of active  
XX Factor VIII:C deficiency in a mammal. The analogues may be used as  
XX immunogens to raise antibodies, and in the treatment of haemophilias, by  
XX improvement of haemostasis. The analogues are resistant to proteolytic  
XX cleavage and display increased plasma half-life. They may be administered  
XX at lower dosages and by different modes of administration.  
SQ Sequence 2352 AA:  
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;  
QY 1 MQEISTGCFEFLCLRFCEFSATRRYYGAVELSDWYMSDGLCELPVDAKPPVPRVPSFPN 60  
DB 1 MQEISTGCFEFLCLRFCEFSATRRYYGAVELSDWYMSDGLCELPVDAKPPVPRVPSFPN 60  
QY 61 TSVVYKTLFEVETDHLFNIAKRPVPMGLGPTIOAEVYDVTAVITLKKMAHSPVSLHAV 120  
DB 61 TSVVYKTLFEVETDHLFNIAKRPVPMGLGPTIOAEVYDVTAVITLKKMAHSPVSLHAV 120  
QY 121 GVSVMKASRGAAYDQTSQREKDDKVPFGSGSHYVQVYKNGKPNASDPLCLTYSYLSH 180  
DB 121 GVSVMKASRGAAYDQTSQREKDDKVPFGSGSHYVQVYKNGKPNASDPLCLTYSYLSH 180  
QY 181 VDLVKNLSGLIGALLVCRGSLAKERTTLLKFTLLPVPFDEGKSMHSETNLSMODRD 240  
DB 181 VDLVKNLSGLIGALLVCRGSLAKERTTLLKFTLLPVPFDEGKSMHSETNLSMODRD 240

Db 181 VDLKDLNSGLIGALLVCREGSLAKEKTQTLAKE ILLFAVFBGSKSMHSETKNSLMODRD 240  
Qy 241 AASARAMPKMHVNGVYVNSRLPGLIGCHRSKVYWHVIGMGTPEVHISFLEBHTFLVRN- 299  
Db 241 AASARAMPKMHVNGVYVNSRLPGLIGCHRSKVYWHVIGMGTPEVHISFLEBHTFLVRN 300  
Qy 300 HROASLEISPTFLTAQTLMDLGOFLFCHISSHGDHGMVAVKVDSCPEEPOLRMKN 359  
Db 301 HROASLEISPTFLTAQTLMDLGOFLFCHISSHGDHGMVAVKVDSCPEEPOLRMKN 360  
Qy 360 BEADEDYDDDLTDSBMVYVRFDDNSPFIOTRSYAKKHPTWYHTAAEEDMDYAEVL 419  
Db 361 BEADEDYDDDLTDSBMVYVRFDDNSPFIOTRSYAKKHPTWYHTAAEEDMDYAEVL 420  
Qy 420 APDRSTKSOYLNNGPORIGRKKYKVRPMATDETEKTRBAIQHESGILLGYEYGD 479  
Db 421 APDRSTKSOYLNNGPORIGRKKYKVRPMATDETEKTRBAIQHESGILLGYEYGD 480  
Qy 480 LLIFKNOASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDPILBGEIFKKYKMTVEEDG 539  
Db 481 LLIFKNOASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDPILBGEIFKKYKMTVEEDG 540  
Qy 540 PTKSDPRLCTRYYSFVNNMERDLASGLIGPLLICYKESYDQNGNOIMSDKNVILFVFD 599  
Db 541 PTKSDPRLCTRYYSFVNNMERDLASGLIGPLLICYKESYDQNGNOIMSDKNVILFVFD 600  
Qy 600 ENRSWYLTENIORFLPRPAGVLEDPERQASNIHMSINGVYEDSLQSVCLHEVAYWIL 659  
Db 601 ENRSWYLTENIORFLPRPAGVLEDPERQASNIHMSINGVYEDSLQSVCLHEVAYWIL 660  
Qy 660 SIGAOTDELVSFESGTYFKHKMYEDTLTLFPFSGETVFSMENBGLMILCHNSDPRNR 719  
Db 661 SIGAOTDELVSFESGTYFKHKMYEDTLTLFPFSGETVFSMENBGLMILCHNSDPRNR 720  
Qy 720 GMTALLKVSCKDKTGDYEDSYEDIISAYLLSKNNALIEPFSQNSRHPSTROKOFANNT 779  
Db 721 GMTALLKVSCKDKTGDYEDSYEDIISAYLLSKNNALIEPFSQNSRHPSTROKOFANNT 780  
Qy 780 IPENDIEKTDPMFARHPKPKTONVSSDILLMLROSPTRHGISLSLDOEAKYETFSDDP 839  
Db 781 IPENDIEKTDPMFARHPKPKTONVSSDILLMLROSPTRHGISLSLDOEAKYETFSDDP 840  
Qy 840 SPGAIOSNNLSSEKTHERPQLHHSQDMVFTPESGLOLRLEKLGTTAAATELKKLDPKVSS 899  
Db 841 SPGAIOSNNLSSEKTHERPQLHHSQDMVFTPESGLOLRLEKLGTTAAATELKKLDPKVSS 900  
Qy 900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMVPHYSQLODTTLFGKKSPLTESGGPLISE 959  
Db 901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMVPHYSQLODTTLFGKKSPLTESGGPLISE 960  
Qy 960 ENNDKLLSEGLMNSOESSMGKNVSTESGRLFKGRABRPALLITDNAMEKVSILKLT 1019  
Db 961 ENNDKLLSEGLMNSOESSMGKNVSTESGRLFKGRABRPALLITDNAMEKVSILKLT 1020  
Qy 1020 NKTSMNSATNKRTHIDGPSLLIENSPYVONILDESDEFEKVTPLIHDMMLDKNATAALR 1079  
Db 1021 NKTSMNSATNKRTHIDGPSLLIENSPYVONILDESDEFEKVTPLIHDMMLDKNATAALR 1080  
Qy 1080 LNHMSNKTSSKNMENVQOKKEGPIPPDAONPDMSPFKMLFLPESARWIORTHGKNSLNS 1139  
Db 1081 LNHMSNKTSSKNMENVQOKKEGPIPPDAONPDMSPFKMLFLPESARWIORTHGKNSLNS 1140  
Qy 1140 GOGSPKOLVSLGPEKSVBEGONPLSEKKNVYVGGETKRYGLAKEMVFPSSANFLTNLD 1199  
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Qy 1200 NLHENHNOEKKIOEBIEKKEETLLOENVVLPJOIHTVGTGRNPKMLFLSTRONVGSY 1259  
Db 1201 NLHENHNOEKKIOEBIEKKEETLLOENVVLPJOIHTVGTGRNPKMLFLSTRONVGSY 1260  
Qy 1260 DGAVAPVLODRSLNDSNTNRTKHTAFHSKKGEEENLEGGNTOKOIYEKAACTTRISPN 1319  
Db 1261 DGAVAPVLODRSLNDSNTNRTKHTAFHSKKGEEENLEGGNTOKOIYEKAACTTRISPN 1320

Qy 1320 TSOONFVTOBSKRAKLOERLPLEETLEKRI IVDSTOWSKNMKHLTPSTLQIDYNEK 1379  
Db 1321 TSOONFVTOBSKRAKLOERLPLEETLEKRI IVDSTOWSKNMKHLTPSTLQIDYNEK 1380  
Qy 1380 EKGATIOSPLSDCLTRSHSIPQANSPPIAKVSSPSPRIYTLRVLFODNSHLPAS 1439  
Db 1381 EKGATIOSPLSDCLTRSHSIPQANSPPIAKVSSPSPRIYTLRVLFODNSHLPAS 1440  
Qy 1440 YRKDSGVOSSSHFLQAGAKNNLSIALITLLEMTGDQREVSGLSFATNSYTKKVENTVL 1499  
Db 1441 YRKDSGVOSSSHFLQAGAKNNLSIALITLLEMTGDQREVSGLSFATNSYTKKVENTVL 1500  
Qy 1500 PKPDLPTSGKVELPKVHIYOKDLFPETFSNOSPQHIDLVGSLQGTGSAIKMNEAR 1559  
Db 1501 PKPDLPTSGKVELPKVHIYOKDLFPETFSNOSPQHIDLVGSLQGTGSAIKMNEAR 1560  
Qy 1560 PGKVPFLRVATESSAKTPSKLLDPLANDNHYGTQIPEEBKSOEKSPEKTAFFKKDTILS 1619  
Db 1561 PGKVPFLRVATESSAKTPSKLLDPLANDNHYGTQIPEEBKSOEKSPEKTAFFKKDTILS 1620  
Qy 1620 LNACESNHAIATAINEGONKPELEVTMAKOGRTBRLCSQNPVLKRRHOREITRTTLODGE 1679  
Db 1621 LNACESNHAIATAINEGONKPELEVTMAKOGRTBRLCSQNPVLKRRHOREITRTTLODGE 1680  
Qy 1680 EIDYDOTTIVEMKKEFDIYDEDEKQSPFOKKTNRHTAAVERLMDYGMSSPHVLRN 1739  
Db 1681 EIDYDOTTIVEMKKEFDIYDEDEKQSPFOKKTNRHTAAVERLMDYGMSSPHVLRN 1740  
Qy 1740 RAQSGSVPOFKKVVPOEFTDGSFTOPLRGELNBHGLGPIYRAVEDNIMVTFRNQAS 1799  
Db 1741 RAQSGSVPOFKKVVPOEFTDGSFTOPLRGELNBHGLGPIYRAVEDNIMVTFRNQAS 1800  
Qy 1800 RPYFSYSLIYSEEDROGAEPRKRFVYVNETTYTFMKVOHNMATKDEPFCQKAAVFSO 1859  
Db 1801 RPYFSYSLIYSEEDROGAEPRKRFVYVNETTYTFMKVOHNMATKDEPFCQKAAVFSO 1860  
Qy 1860 VDLERKDHSLIGPLLYCHTNTLNAHROVYVOEBALEFTTJEDETKSNYTEMENR 1919  
Db 1861 VDLERKDHSLIGPLLYCHTNTLNAHROVYVOEBALEFTTJEDETKSNYTEMENR 1920  
Qy 1920 APCNIOEDEDPEKENYRPHAINGYIMDTLPGLVMAODORIIMVLLSMGSENNIHSIHFSO 1979  
Db 1921 APCNIOEDEDPEKENYRPHAINGYIMDTLPGLVMAODORIIMVLLSMGSENNIHSIHFSO 1980  
Qy 1980 HFTVYRKKEEYKMAALYNLPGVFETVEMLDSKAGIWRVCELIGEHLHAGMSTLFLVYSNK 2039  
Db 1981 HFTVYRKKEEYKMAALYNLPGVFETVEMLDSKAGIWRVCELIGEHLHAGMSTLFLVYSNK 2040  
Qy 2040 COTPLGMASGHIBDPOITASGOYGMAPKILARLHYSGSINAMSTKEPSMTKXVDLAPMT 2099  
Db 2041 COTPLGMASGHIBDPOITASGOYGMAPKILARLHYSGSINAMSTKEPSMTKXVDLAPMT 2100  
Qy 2100 IHGIRTOGARQKFSLLYSOFTIMYSLDGKRWOTYKGNSTGTLMVFGVNDSSGIRKHNTP 2159  
Db 2101 IHGIRTOGARQKFSLLYSOFTIMYSLDGKRWOTYKGNSTGTLMVFGVNDSSGIRKHNTP 2160  
Qy 2160 NPPIIARIYLRHPTHSIRSTLRMEIMCCLDSCSMPMLMESKAISDQOITASSYFTNNF 2219  
Db 2161 NPPIIARIYLRHPTHSIRSTLRMEIMCCLDSCSMPMLMESKAISDQOITASSYFTNNF 2220  
Qy 2220 ATWSPSKARLHLOGRSNANRPQVNNPKRMHLDPOFTKMYVTVYTOGYKSLTYSMYKEE 2279  
Db 2221 ATWSPSKARLHLOGRSNANRPQVNNPKRMHLDPOFTKMYVTVYTOGYKSLTYSMYKEE 2280  
Qy 2280 LISSODGHOWTLFQNGKVVKVFQGNDSFTPVVNSLDBPLLJTRYLRTHPOSVWHQIALR 2339  
Db 2281 LISSODGHOWTLFQNGKVVKVFQGNDSFTPVVNSLDBPLLJTRYLRTHPOSVWHQIALR 2340  
Qy 2340 MEVLGCEADOLY 2351  
Db 2341 MEVLGCEADOLY 2352

RESULT 63  
AAAM1372  
ID AAAM1372 standard; Protein: 2352 AA.  
XX  
AC AAAM1372;  
XX  
DT 18-NOV-1997 (first entry)  
XX  
DE Active Factor VIII:C analogue residue 336 P insertion.  
XX  
KW Factor VII:C; analogue; glycoprotein; blood coagulation cascade;  
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KW plasma protease; thrombin; immunogen; antibody; haemophilia; therapy;  
KW proteolytic cleavage.  
XX  
OS Homo sapiens.  
XX Synthetic.  
XX  
FH Key Location/Qualifiers  
FT Peptide 1..19  
FT /note= "signal peptide"  
FT Protein 20..2352  
FT /note= "mature Factor VIII:C"  
FT Region 20..1668  
FT /note= "heavy chain fragment"  
FT Misc-difference 355  
FT /note= "inserted residue"  
FT Region 1669..2351  
FT /note= "light chain fragment"  
FT Domain 761..1668  
FT /note= "B domain"  
XX  
PN W09J03195-A1.  
XX  
PD 30-JAN-1997.  
XX  
PF 09-JUL-1996; 96WO-US11444.  
XX  
PR 11-JUL-1995; 95US-0001025.  
XX  
PA (CHIR ) CHIRON CORP.  
XX  
PI Cohen FE, Hung DT, Innis M;  
XX WPI: 1997-119050/11.  
DR  
XX  
FT Factor VIII:C analog modified adjacent to a non-activating Arg  
FT residue - used in the treatment of haemophiliacs, by improvement of  
FT haemostasis  
XX  
PS Claim 17; Page -: 90pp; English.

XX Sequence 2352 AA.  
SQ  
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;  
QY 1 MQLSTCEFLCLRFCEFSATRRYYLGAVALSMWQMSDGLCELPVDAFPFPRKSPFPN 60  
DB 1 MQLSTCEFLCLRFCEFSATRRYYLGAVALSMWQMSDGLCELPVDAFPFPRKSPFPN 60  
QY 61 TSVYKKTLEVFETHTLEFNIAKPPPPMGLPPTIOAVYPTVITTKNMAHPVSLAV 120  
DB 61 TSVYKKTLEVFETHTLEFNIAKPPPPMGLPPTIOAVYPTVITTKNMAHPVSLAV 120  
QY 121 GVSYKASBGALEYDQTSQREKEDKVPFGSHYVWOLKENGPMASDPLCLTYSLSH 180  
DB 121 GVSYKASBGALEYDQTSQREKEDKVPFGSHYVWOLKENGPMASDPLCLTYSLSH 180  
QY 181 VDLVKDLSGLIGALLVCREGLAKERTQTLHKFTLLFAVDEGKSMHSETKNSLMODRD 240  
DB 181 VDLVKDLSGLIGALLVCREGLAKERTQTLHKFTLLFAVDEGKSMHSETKNSLMODRD 240  
QY 241 AASARAPKMHVNGVYVNRSLDGLICHRKSYVWVIGMTPEVHSIFLEGTFVLVNH 300  
DB 241 AASARAPKMHVNGVYVNRSLDGLICHRKSYVWVIGMTPEVHSIFLEGTFVLVNH 300  
QY 301 KQSLFISPTFLTQTLMDLQGLFLFCHISSHQHDMEXYVNDSCPEPQL-RMKNN 359  
DB 301 KQSLFISPTFLTQTLMDLQGLFLFCHISSHQHDMEXYVNDSCPEPQL-RMKNN 360  
QY 360 EEAEDYDDDLTDEMDVVRDDDNPSFQIIRSVAKKHPTKWVYIAEEEDMDYAPLVL 419  
DB 360 EEAEDYDDDLTDEMDVVRDDDNPSFQIIRSVAKKHPTKWVYIAEEEDMDYAPLVL 420  
QY 420 APDRSKSQYLNNGPQIRGRKYKVFMAVYDDEFKTRREALIQHESGILGLPLYGEVDT 479  
DB 420 APDRSKSQYLNNGPQIRGRKYKVFMAVYDDEFKTRREALIQHESGILGLPLYGEVDT 480  
QY 480 LLIIFPKNOASRPYNIYPGIDTVPRLYSRLKGYKHKDKPILPGIFRYKMYVTYVDS 539  
DB 480 LLIIFPKNOASRPYNIYPGIDTVPRLYSRLKGYKHKDKPILPGIFRYKMYVTYVDS 540  
QY 540 PTKSDPRLCTRYSSEFVNMERDLASGLICPLLICYKESVDGRQNMDSKRVLLFSYVD 599  
DB 540 PTKSDPRLCTRYSSEFVNMERDLASGLICPLLICYKESVDGRQNMDSKRVLLFSYVD 600  
QY 600 ENRSWYLTENIORFLPNFAGVQLEDEPQASNMHSINGVYFDSLQTSVCLHEVAYVYL 659  
DB 600 ENRSWYLTENIORFLPNFAGVQLEDEPQASNMHSINGVYFDSLQTSVCLHEVAYVYL 660  
QY 660 SIGAOTDFLSVFSGYFGRKMYEDTLTFPFSGETVFMENPGIAMLIGCHNSDPFNR 719  
DB 660 SIGAOTDFLSVFSGYFGRKMYEDTLTFPFSGETVFMENPGIAMLIGCHNSDPFNR 720  
QY 720 GNRLLAKVSCCKNKGDYEDSIEDISAVLLSKNNAIPRFSONSHSTOKOPNAT 779  
DB 720 GNRLLAKVSCCKNKGDYEDSIEDISAVLLSKNNAIPRFSONSHSTOKOPNAT 780  
QY 780 IPENDIEKTPFAHRTPMKIQNVSSSLLMLLRQSPFPGSLSDLOEARYEFPSDP 839  
DB 780 IPENDIEKTPFAHRTPMKIQNVSSSLLMLLRQSPFPGSLSDLOEARYEFPSDP 840  
QY 840 SPDAIDNNLSLEMHHPFOLHNSGMYTPPSGQLELNKAGTTAAELKLPFKKYS 899  
DB 840 SPDAIDNNLSLEMHHPFOLHNSGMYTPPSGQLELNKAGTTAAELKLPFKKYS 900  
QY 900 TSNMLSTPSONLAAGDNTSSLGPPSPVAYDSQDLTTLFKKSSPLTEGGPLSSE 959  
DB 900 TSNMLSTPSONLAAGDNTSSLGPPSPVAYDSQDLTTLFKKSSPLTEGGPLSSE 960  
QY 960 ENDSKLEBSGLMNSQESWGMKNVSTESGRLFKGRAGPALLTDNMLFVYSISLKT 1019  
DB 960 ENDSKLEBSGLMNSQESWGMKNVSTESGRLFKGRAGPALLTDNMLFVYSISLKT 1019

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Db      961  EANDSKLLESGIMNSQESSMGKNVSTESGRLEFKGRABGRPALITKDNALFKVSIISLKT  1020
Oy      1020 NKTSMNSATNRKTHIDGSPILLIENSPWOWIIESOTFEKKYTPLIIDHMDMKNAALR  1079
Db      1021 NKTSMNSATNRKTHIDGSPILLIENSPWOWIIESOTFEKKYTPLIIDHMDMKNAALR  1080
Oy      1080 LNHMSNKTSSKNMKNVQOKKGGP1PPDANPDMSFEKMLFLPESARWIOETHGKNLS  1139
Db      1081 LNHMSNKTSSKNMKNVQOKKGGP1PPDANPDMSFEKMLFLPESARWIOETHGKNLS  1140
Oy      1140 GGGSPKQVSLGPEKSVEGONFLSEKKNVVGGEFTKDVGLKEVFPSSRNLEFLNLD  1199
Db      1141 GGGSPKQVSLGPEKSVEGONFLSEKKNVVGGEFTKDVGLKEVFPSSRNLEFLNLD  1200
Oy      1200 NLEHNNTHNOEKKTOEIEIEKKEFLLOEENVLPOLHVTGTRKNMKMLFLSTRONVGSY  1259
Db      1201 NLEHNNTHNOEKKTOEIEIEKKEFLLOEENVLPOLHVTGTRKNMKMLFLSTRONVGSY  1260
Oy      1260 DGAVAPVLQDERSLNDSTNRKHTAHFSKKGEENLEGLNOTKOIYEKYACTTRISPN  1319
Db      1261 DGAVAPVLQDERSLNDSTNRKHTAHFSKKGEENLEGLNOTKOIYEKYACTTRISPN  1320
Oy      1320 TSOQNFVTOQRKRALKOFRLPLEETELKRIITVDISTOKSKMKHLPPSTLTODIYNEK  1379
Db      1321 TSOQNFVTOQRKRALKOFRLPLEETELKRIITVDISTOKSKMKHLPPSTLTODIYNEK  1380
Oy      1380 EKGAITOSPISDCLTNRSHSIPQANSPLPIAKVSSPISPIYTLRVLPFODNSHLPAAS  1439
Db      1381 EKGAITOSPISDCLTNRSHSIPQANSPLPIAKVSSPISPIYTLRVLPFODNSHLPAAS  1440
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Db      1441 YRRKDSGVQESSHFLQAKKNNLSLAILLEMTDQOEVSGLQTSATNSVYKKEVNTVL  1500
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Db      1501 PKPDLPTSGKVELLPVHLYOKDLPEPTNSGSPGLDIVEGSLLOGEGAIKMNENR  1560
Oy      1560 PKGVPLFVLVATESAKTPSKLDPLAMDNHGTQIPREKKSQEKSPKTAKKKDTILS  1619
Db      1561 PKGVPLFVLVATESAKTPSKLDPLAMDNHGTQIPREKKSQEKSPKTAKKKDTILS  1620
Oy      1620 LNACESNHAIAINEGONKPEIEVTWAKQTERLCSQNPVLKRHQREITRTTLOSPOE  1679
Db      1621 LNACESNHAIAINEGONKPEIEVTWAKQTERLCSQNPVLKRHQREITRTTLOSPOE  1680
Oy      1680 EIDYDITISYEMKEDDIYDEENOSPRFOKTRHYFTAAYERLMDYGSSSPHYLNR  1739
Db      1681 EIDYDITISYEMKEDDIYDEENOSPRFOKTRHYFTAAYERLMDYGSSSPHYLNR  1740
Oy      1740 RAQSSVPQFKKVVFOFTDGSFTQPLRGELNHLGLGLGPTIRAEVEDNIMVTRNOAS  1799
Db      1741 RAQSSVPQFKKVVFOFTDGSFTQPLRGELNHLGLGLGPTIRAEVEDNIMVTRNOAS  1800
Oy      1800 RPYSEYSSLSIYEDROGAEPKRNVPNETKTYFMKVOHNAPTKDEFDKAMAYFSD  1859
Db      1801 RPYSEYSSLSIYEDROGAEPKRNVPNETKTYFMKVOHNAPTKDEFDKAMAYFSD  1860
Oy      1860 VDLEKDVHSGLIGPLVCHNTNLPAGHROTVQOEPALFTIPDETksYFENNERCR  1919
Db      1861 VDLEKDVHSGLIGPLVCHNTNLPAGHROTVQOEPALFTIPDETksYFENNERCR  1920
Oy      1920 ARCNIOEMDPTFKENYFHAINGYIMDTPLGLVNAQOQRIKRWLLSMGSENEIHSIHSG  1979
Db      1921 ARCNIOEMDPTFKENYFHAINGYIMDTPLGLVNAQOQRIKRWLLSMGSENEIHSIHSG  1980
Oy      1980 HVTYVRKKEEYKMAVLYNYPGVEFVEMLPKSAIIMRVECLIGEBHLHAGMSTLFLVYSNK  2039
Db      1981 HVTYVRKKEEYKMAVLYNYPGVEFVEMLPKSAIIMRVECLIGEBHLHAGMSTLFLVYSNK  2040
Oy      2040 COTPLGMAIGHIRDFQITASGOYQOWAPLARLHYSSSIAMSTKPEPFMIVDLAPMI  2099
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Oy      2100 IHGIKTOGAROKRSSLYISQFIIMYSLDGKKNOTYRGSTGTLMPFGNDSSGIRKNIF  2159
Db      2101 IHGIKTOGAROKRSSLYISQFIIMYSLDGKKNOTYRGSTGTLMPFGNDSSGIRKNIF  2160
Oy      2160 NPPIIARYIRLAPTHYSIRSTLRMLMCCDLNSCSMPLMESKALISDAQITASSYFTNMF  2219
Db      2161 NPPIIARYIRLAPTHYSIRSTLRMLMCCDLNSCSMPLMESKALISDAQITASSYFTNMF  2220
Oy      2220 ATWSPSKARLHLQGRSNMARPQVNNPKEMLOVDPOKTMKVGTGTVQVKSILTSMYVKEF  2279
Db      2221 ATWSPSKARLHLQGRSNMARPQVNNPKEMLOVDPOKTMKVGTGTVQVKSILTSMYVKEF  2280
Oy      2280 LISSQOGHOMTLEFQNGKVKYKFGQNDSTFPVYNSLDPLLTRLRTHRPQSWHYQIALR  2339
Db      2281 LISSQOGHOMTLEFQNGKVKYKFGQNDSTFPVYNSLDPLLTRLRTHRPQSWHYQIALR  2340
Oy      2340 MEVLGCEADOLY 2351
Db      2341 MEVLGCEADOLY 2352

RESULT 64
AAW11342
ID  AAW11342 standard; Protein, 2352 AA.
XX
AC  AAW11342:
XX
DT  17-NOV-1997 (first entry)
XX
DE  Active Factor VIII:C analogue residue 224 F/E/P insertion.
XX
KW  Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW  fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW  plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;
KW  proteolytic cleavage.
XX
OS  Homo sapiens.
XX
SX  Synthetic.
XX
FH  Key
FH  Peptide
FT  /note= "1..19
FT  /note= "signal peptide"
FT  /note= "20..2352
FT  /note= "mature Factor VIII:C"
FT  /note= "20..1668
FT  /note= "heavy chain fragment"
FT  Modified-site
FT  /label= Phe, Glu, Pro
FT  /note= "inserted residue"
FT  /note= "1669..2351
FT  /note= "light chain fragment"
FT  /note= "761..1668
FT  /note= "B domain"
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MO9703195..A1.
XX
PD  30-JAN-1997.
XX
PE  09-JUL-1996; 96MO-US11444.
XX
PR  11-JUL-1995; 95US-0001025.
XX
PA  (CHIR ) CHIRON CORP.
PI  Cohen FE, Hung DT, Innis M;
XX  WPI; 1997-119050/11.
XX
PT  Factor VIII:C analog modified adjacent to a non-activating Arg
PT  residue - used in the treatment of haemophiliacs, by improvement of
PT  haemostasis
XX

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PS Claim 10; Page -: 90pp; English.

CC AM11330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see A451357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC peptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophilia, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.

XX Sequence 2352 AA;

Query Match 99.9%; Score 12407.5; DB 18; Length 2352;

Best Local Similarity 100.0%; Pred. No. 0;

Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

QY 1 MOELSTCFCLLRCSFATRRYLGAVELSMYMOGDLGPVADAPPRPVKSPFN 60  
DB 1 MOELSTCFCLLRCSFATRRYLGAVELSMYMOGDLGPVADAPPRPVKSPFN 60  
QY 61 TSVYTKTLVEETDHLFNIAKPRPPWGLGPTIOAEYDYVYITLKMASSPVSLHAY 120  
DB 61 TSVYTKTLVEETDHLFNIAKPRPPWGLGPTIOAEYDYVYITLKMASSPVSLHAY 120  
QY 121 GVSYWKASGEAEYDDQTSQREKEDKVPGGSHYVQVLKENGPMASDPLCLTYSLASH 180  
DB 121 GVSYWKASGEAEYDDQTSQREKEDKVPGGSHYVQVLKENGPMASDPLCLTYSLASH 180  
QY 181 VDLVMDLNSGLIGLALVCRGSLAKEKQTQHTKLTLLFAVFDGKSMHSEKNSLMODRD 240  
DB 181 VDLVMDLNSGLIGLALVCRGSLAKEKQTQHTKLTLLFAVFDGKSMHSEKNSLMODRD 240  
QY 241 AAS-ARAPKMHYNGYVNSLPGLIGCHKRSYVHWYTGTTPEVHSFTLEGHTFLVRN 299  
DB 241 AAS-ARAPKMHYNGYVNSLPGLIGCHKRSYVHWYTGTTPEVHSFTLEGHTFLVRN 299  
QY 300 HROASLEISPTTFEFAEGLMLDLGQFLFCHISSHODGMEAVYKVDSCPEEPOLRMKN 359  
DB 300 HROASLEISPTTFEFAEGLMLDLGQFLFCHISSHODGMEAVYKVDSCPEEPOLRMKN 359  
QY 360 FEAEYDDDLDSMDVYPRDDNSPFTQIRSAKPKPTWYHIAAEEDMDAPLYL 419  
DB 360 FEAEYDDDLDSMDVYPRDDNSPFTQIRSAKPKPTWYHIAAEEDMDAPLYL 419  
QY 420 APDRSYKSOYLNNGPQIRGKRYKVRMAVYDTEFTREAIQIHESGILGPLYLGEVDT 479  
DB 420 APDRSYKSOYLNNGPQIRGKRYKVRMAVYDTEFTREAIQIHESGILGPLYLGEVDT 479  
QY 480 LLIIFKNQASRPYNIYPHGITYVRPLYSRRLPKVKVHLKDFPLIPELIRKYKWTYEDG 539  
DB 480 LLIIFKNQASRPYNIYPHGITYVRPLYSRRLPKVKVHLKDFPLIPELIRKYKWTYEDG 539  
QY 540 PTKSDPCLTRYYSYFNMERDLASGLIGLLTCYKESVQGRQNMJSKRNVILFSYFD 599  
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QY 600 ENRSWYLTENTQRLPNPAGVLEDPERQASINMHSINGYVFDSDLSVCLHEVAYWYIL 659  
DB 600 ENRSWYLTENTQRLPNPAGVLEDPERQASINMHSINGYVFDSDLSVCLHEVAYWYIL 659  
QY 601 ENRSWYLTENTQRLPNPAGVLEDPERQASINMHSINGYVFDSDLSVCLHEVAYWYIL 660  
DB 601 ENRSWYLTENTQRLPNPAGVLEDPERQASINMHSINGYVFDSDLSVCLHEVAYWYIL 660

QY 660 SIGAOTDLVSFSGYTERHKRVYEDTLTLPSSGETVFMSENENBGLMILGCHNSDFNR 719  
DB 661 SIGAOTDLVSFSGYTERHKRVYEDTLTLPSSGETVFMSENENBGLMILGCHNSDFNR 720  
QY 720 GMTALLVSSCDKNTGDYEDSYEDIISAYLISKNNAIEPRFSQNSRHPSTROKORNAT 779  
DB 721 GMTALLVSSCDKNTGDYEDSYEDIISAYLISKNNAIEPRFSQNSRHPSTROKORNAT 780  
QY 780 IPEMDIKTPWFARHTPMPKIONVSSDILMLLRSPPHGLISLDOAEKYEFTSDDP 839  
DB 781 IPEMDIKTPWFARHTPMPKIONVSSDILMLLRSPPHGLISLDOAEKYEFTSDDP 840  
QY 840 SPGAIDSNLSLMEHTFRPQOLHSGDVFTEPSGLOLRLNEKLTGAATBELKLDPRVSS 899  
DB 841 SPGAIDSNLSLMEHTFRPQOLHSGDVFTEPSGLOLRLNEKLTGAATBELKLDPRVSS 900  
QY 900 TSNNLITIPSDMLAAGTDNTSSLGPPSPMVHYDSOLDTTLFGKKSPLTESGAPLSLE 959  
DB 901 TSNNLITIPSDMLAAGTDNTSSLGPPSPMVHYDSOLDTTLFGKKSPLTESGAPLSLE 960  
QY 960 ENDSKLESGLNNSQESGKNNVSTESGRLEFKRARGPALLTKMALPKYSISLMT 1019  
DB 961 ENDSKLESGLNNSQESGKNNVSTESGRLEFKRARGPALLTKMALPKYSISLMT 1020  
QY 1020 NKTNSNATRKTHIDGPSLITENSPSYMONILESDEKRVYPLIHDRMLMDKNATLR 1079  
DB 1021 NKTNSNATRKTHIDGPSLITENSPSYMONILESDEKRVYPLIHDRMLMDKNATLR 1080  
QY 1080 LNHMSNKTSSKNMEVQOKKRGPIPPDAQNPMSFFKMLFPESARMIQRTGKNSLNS 1139  
DB 1081 LNHMSNKTSSKNMEVQOKKRGPIPPDAQNPMSFFKMLFPESARMIQRTGKNSLNS 1140  
QY 1140 GQSPSPQOLVSLGPEKSYGVGNFLSEKKNVYKGGFTDVGLEKMPSPSRNLFLEND 1199  
DB 1141 GQSPSPQOLVSLGPEKSYGVGNFLSEKKNVYKGGFTDVGLEKMPSPSRNLFLEND 1200  
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DB 1201 NIHEMNTHNOEKKIOBEIEKFTLLIOENVVLPQIHVTGTHKPKNLFLELSTONVBSY 1260  
QY 1260 DGAYAPVLDQFRSLNOSTNRTKHTAHFSKGBENLELGNOTQOIEKYACTTRISPN 1319  
DB 1261 DGAYAPVLDQFRSLNOSTNRTKHTAHFSKGBENLELGNOTQOIEKYACTTRISPN 1320  
QY 1320 TSOONFVTOBSKALQOPRLPELETELEKRTIYDQSTQSKNMKHLPSFTLIOYDNK 1379  
DB 1321 TSOONFVTOBSKALQOPRLPELETELEKRTIYDQSTQSKNMKHLPSFTLIOYDNK 1380  
QY 1380 EKGALITQPLSDCLTRSHSIPQANSPLPAKVSSPSTIRPYLTRVLFDONSSHLPAS 1439  
DB 1381 EKGALITQPLSDCLTRSHSIPQANSPLPAKVSSPSTIRPYLTRVLFDONSSHLPAS 1440  
QY 1440 YRKXDSGVQSSHFLOGAKKNLSLALITLTEMGDQREVSIGTSATNSVYKKVEVTVL 1499  
DB 1441 YRKXDSGVQSSHFLOGAKKNLSLALITLTEMGDQREVSIGTSATNSVYKKVEVTVL 1500  
QY 1500 EKPDLPTSGKVELLEKVTYKOLPEFTESNSPGHLDLVGCSLQSTBEAIAKMNANR 1559  
DB 1501 EKPDLPTSGKVELLEKVTYKOLPEFTESNSPGHLDLVGCSLQSTBEAIAKMNANR 1560  
QY 1560 PKQVPELVATSSSACTPSKLDPLAMDNHGQIQIREKMSQESKPEKTAFFKKKDTILS 1619  
DB 1561 PKQVPELVATSSSACTPSKLDPLAMDNHGQIQIREKMSQESKPEKTAFFKKKDTILS 1620  
QY 1620 LNACESNHAIATINEONKPELEVMWAQGTRELSQNPVLKRRHOREITRTLOSQOE 1679  
DB 1621 LNACESNHAIATINEONKPELEVMWAQGTRELSQNPVLKRRHOREITRTLOSQOE 1680  
QY 1680 ETDYDDTISVEMKKEFDIYDENQSRFSQKTRHYTIAAVERLMDYGSSSPHYLRN 1739  
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QY 1740 RAQSGSVQFKKVVQEFDTGDSFTQPLRYGELNEHLGLGPIRAEVEDNIMTYFRMQAS 1799  
DB 1740 RAQSGSVQFKKVVQEFDTGDSFTQPLRYGELNEHLGLGPIRAEVEDNIMTYFRMQAS 1799

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DB 1741 RAQSGSVQFQKKVVFQFETDGSFTQPLRNGELNEHLGLPTIRAEVENIMVTFRNQAS 1800
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DB 1801 RPYSTSSLSIYEEDDQGAEPKRFVKNETKTYFMKVOHMAPTKDEEDCKAMAYFSD 1860
QY 1860 VLEKDVHSGLIGPLVCHNTLNPAHQVYQVEAFLEFTIDEKRSYFTENNERNCR 1919
DB 1861 VLEKDVHSGLIGPLVCHNTLNPAHQVYQVEAFLEFTIDEKRSYFTENNERNCR 1920
QY 1920 APCNOMEDPTEKENYEFHAINCYIMDPLRGVMAOORIRMYLISGNSNEMHSHIRSG 1979
DB 1921 APCNOMEDPTEKENYEFHAINCYIMDPLRGVMAOORIRMYLISGNSNEMHSHIRSG 1980
QY 1980 HVEFYVKKKEKYMALYNLPGEVEFVEMLPKACIMRVECLIGEBLHAGMSTFLVYSNK 2039
DB 1981 HVEFYVKKKEKYMALYNLPGEVEFVEMLPKACIMRVECLIGEBLHAGMSTFLVYSNK 2040
QY 2040 CQPLGMAHGHIRDFQITASGQYGQWAPKLARLHYSGSINAMSTKPEFMIKVLLAPMI 2099
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DB 2101 HGKITGAKROKESLTIOSFTIMYGLDCKKQYRNGSTGLMVFPGVDSGIKHMF 2160
QY 2160 NPPIIARYIRLHPHYISIRSTLMELMGCDLNSGMPLGMSKRAISDAQITASSYFTNMF 2219
DB 2161 NPPIIARYIRLHPHYISIRSTLMELMGCDLNSGMPLGMSKRAISDAQITASSYFTNMF 2220
QY 2220 ATWSPSKARLHLOGRSNAMPQVNNPKEMIQDFQTKYVGYTQGVSLTSMYKEEF 2279
DB 2221 ATWSPSKARLHLOGRSNAMPQVNNPKEMIQDFQTKYVGYTQGVSLTSMYKEEF 2280
QY 2280 LTISSQDGHQMTLFFQNGKXKVFQGNQDSFTYVNSLIDPLLRIRIRHPOSWVQIOLR 2339
DB 2281 LTISSQDGHQMTLFFQNGKXKVFQGNQDSFTYVNSLIDPLLRIRIRHPOSWVQIOLR 2340
QY 2340 MEYLAGEADOLY 2351
DB 2341 MEYLAGEADOLY 2352

RESULT 65
AAM1344
ID AAM1344 standard; Protein: 2352 AA.
AC AAM1344:
XX
XX
XX 17-NOV-1997 (first entry)
DE Active Factor VIII:C analogue residue 249 P insertion.
XX
XX
XX
XX
XX Factor VIII:C analogue: glycoprotein; blood coagulation cascade;
KM fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KM plasma protease; thrombin; immunogen; antibody; haemophilia; therapy;
XX proteolytic cleavage.
XX
XX Homo sapiens.
OS Synthetic.
XX
XX
XX Key Location/Qualifiers
FH Peptide 1..19
FT /note= "signal peptide"
FT Protein 20..2352
FT /note= "mature Factor VIII:C"
FT Region 20..1668
FT /note= "heavy chain fragment"
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FT Region /note= "light chain fragment"
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XX
XX 09-JUL-1996; 96MO-US11444.
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XX 11-JUL-1995; 95US-0001025.
XX
XX (CHIR ) CHIRON CORP.
XX
XX Cohen EE, Hung DT, Innis M;
XX WPI; 1997-119050/11.
XX
XX Factor VIII:C analog modified adjacent to a non-activating Arg
PT residue - used in the treatment of haemophilias, by improvement of
PT haemostasis
XX
XX Claim 11; Page -: 90pp; English.
XX
XX AAM1330-M11472 represent active Factor VIII:C analogues of the
CC invention. These sequences were created by mutating the wild type Factor
CC VIII:C coding sequence (see AAT91357) using mutagenic primers. The
CC analogues comprise a native Factor VIII:C polypeptide modified at a site
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC dipeptide is created. Factor VIII:C is a large glycoprotein that
CC participates in the blood coagulation cascade that ultimately converts
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC X-chromosome-linked inherited bleeding diathesis, haemophilia A, which is an
CC mature polypeptide is cleaved to generate heavy and light chain fragments
CC that are further cleaved. Complexes of two or more of the analogues,
CC nucleic acids and vectors encoding them may be used alone or in
CC conjunction with each other, for the prevention or treatment of active
CC Factor VIII:C deficiency in a mammal. The analogues may be used as
CC immunogens to raise antibodies, and in the treatment of haemophilias, by
CC cleavage and display increased plasma half-life. They may be administered
CC at lower dosages and by different modes of administration.
XX
XX
XX Sequence 2352 AA:
SQ
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;
Best Local Similarity 100.0%; Pred. No. 0;
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;
QY 1 MOLESTCFELCLARCFESATRRYYLGAVELSNYMNOSDGLPVDARPPRRVRSFPFN 60
DB 1 MOLESTCFELCLARCFESATRRYYLGAVELSNYMNOSDGLPVDARPPRRVRSFPFN 60
QY 61 TSVVYKKTLPVEFTDHLFNIAKRPMPMGLLPPTQAEVYDVYVITLKMAHSHVSLHAY 120
DB 61 TSVVYKKTLPVEFTDHLFNIAKRPMPMGLLPPTQAEVYDVYVITLKMAHSHVSLHAY 120
QY 62 TSVVYKKTLPVEFTDHLFNIAKRPMPMGLLPPTQAEVYDVYVITLKMAHSHVSLHAY 120
DB 62 TSVVYKKTLPVEFTDHLFNIAKRPMPMGLLPPTQAEVYDVYVITLKMAHSHVSLHAY 120
QY 121 GVSYWKASGAEVDDQTSQREKEDKVPFGSGSHYVQVLEKNGPASPCLCTRYSTLSH 180
DB 121 GVSYWKASGAEVDDQTSQREKEDKVPFGSGSHYVQVLEKNGPASPCLCTRYSTLSH 180
QY 181 VDLVYDNLNSGLIGALVLCRGSLAKETQTLAKRTLLFANVPDGSKMSHETKNSLMODRD 240
DB 181 VDLVYDNLNSGLIGALVLCRGSLAKETQTLAKRTLLFANVPDGSKMSHETKNSLMODRD 240
QY 241 AASARAMPKMTVNGVYNSRLPGLICGH-RKSYVWHVIGMTTPEVHSTFLEGHTFLVRN 299
DB 241 AASARAMPKMTVNGVYNSRLPGLICGH-RKSYVWHVIGMTTPEVHSTFLEGHTFLVRN 299
QY 300 HROASTDSPTTPTTAOTLLMDIGOLFECCHISSHODGAEAVKVDSCPEPQRLRKN 359
DB 301 HROASTDSPTTPTTAOTLLMDIGOLFECCHISSHODGAEAVKVDSCPEPQRLRKN 359
```



QY 360 EEAEDYDDDLTDEMDVYFDDDNPSFIQIRSAKKHPTWVHYIAAEEEDMDYAPLV 419  
D 361 EEAEDYDDDLTDEMDVYFDDDNPSFIQIRSAKKHPTWVHYIAAEEEDMDYAPLV 420  
QY 420 APDRSKYKSOYLNNGFORIGRKYKVRPMATYDDETFKTRATOHSGILGELGVEGDT 479  
D 421 APDRSKYKSOYLNNGFORIGRKYKVRPMATYDDETFKTRATOHSGILGELGVEGDT 480  
QY 480 LLIIFKNOASRPYNIYPHGIITDVPYLRPLPKGVKHLKDFPLDPEIIFKTKWTVYEDG 539  
D 481 LLIIFKNOASRPYNIYPHGIITDVPYLRPLPKGVKHLKDFPLDPEIIFKTKWTVYEDG 540  
QY 540 PTKSDPRLCTRYYSFVFNMERDLASGLIGPLILCYKESYDQORNOJMSDKRNVLFSVFD 599  
D 541 PTKSDPRLCTRYYSFVFNMERDLASGLIGPLILCYKESYDQORNOJMSDKRNVLFSVFD 600  
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D 601 EKRSMYLTENIORPLNPAGVOLEDPERQASNIHSHNGYVPSILOSLVCLHEVAWYIL 660  
QY 660 STGAQOTDFLSYFTSGYTFKHKWYEDTLTFPPSGETVPMKMPGLWLGCHNSDRNR 719  
D 661 STGAQOTDFLSYFTSGYTFKHKWYEDTLTFPPSGETVPMKMPGLWLGCHNSDRNR 720  
QY 720 GMTALLKVSCKDKWTG DYEDSYEDISAYLLSKNNAIEPRSFQONSRRPSTROKOFNAT 779  
D 721 GMTALLKVSCKDKWTG DYEDSYEDISAYLLSKNNAIEPRSFQONSRRPSTROKOFNAT 780  
QY 780 IPENDIEKTDPMFPAHPTMPKIQONVSSDGLMLROSPPHGISLSDLOEAKYETFSDDP 839  
D 781 IPENDIEKTDPMFPAHPTMPKIQONVSSDGLMLROSPPHGISLSDLOEAKYETFSDDP 840  
QY 840 SPGAIDSNNSLSEKTHFRPOLHHSQDMVFTPESSLOLRLEKIGTTAATLKKLDYFVSS 899  
D 841 SPGAIDSNNSLSEKTHFRPOLHHSQDMVFTPESSLOLRLEKIGTTAATLKKLDYFVSS 900  
QY 900 TSNNLISIPSDNLAAGTDWTSLSGPMPAPHYVSOQDITLTFGKSSPFTESGGLSISE 959  
D 901 TSNNLISIPSDNLAAGTDWTSLSGPMPAPHYVSOQDITLTFGKSSPFTESGGLSISE 960  
QY 960 ENNDKSLLESGLMNSOESSWGKNVSTESGRLFGKRAHBPALLITDANLFPVYSILKT 1019  
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D 1081 LNHMSNKTTSKKNEMVQOKKEGPIPPDAONPDMSPFKMLFLPESARWIOPTHGKNSLNS 1140  
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D 1141 GGGSPKOLVSLGPEKSVBQONFLSKKNVYVGGFTKVOGLKEMVFPSSNLFLLTMD 1200  
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D 1201 NLHENNTHNOBKKEIOEIEKEKTELIOENVYLPOLHTVGTGNKMKMLFLLSSTRONVEG 1260  
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D 1261 DGATVAVLODPRSLNDSTNRTKHTAHFSKGGEEENLEGLGNOTKOIVKVCATTRISP 1320  
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D 1321 TSQONFVTOQRKALKOFRLPLETELEKRIIVDTSTOWSKMKHLPTSTLOIDYNEK 1380  
QY 1380 EKGALTOSPLSDCLTRSHSIPQANRSPPLIAKVSFSPSIPYLVFLQDNNSHLPAAS 1439  
D 1381 EKGALTOSPLSDCLTRSHSIPQANRSPPLIAKVSFSPSIPYLVFLQDNNSHLPAAS 1440

QY 1440 YRKDSGVQESSHFLQAKKNLSTALLTLEMTGDREVGSIGTSATNSVYKKVENTVL 1499  
D 1441 YRKDSGVQESSHFLQAKKNLSTALLTLEMTGDREVGSIGTSATNSVYKKVENTVL 1500  
QY 1500 PKPDLPTSGKEVELPKVHIYQKDLFPTETSNGPSGHLDLVGSLLOGTGEGAIKMEANR 1559  
D 1501 PKPDLPTSGKEVELPKVHIYQKDLFPTETSNGPSGHLDLVGSLLOGTGEGAIKMEANR 1560  
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D 1681 ETDYDDFTSYEMKKEKEDFYDDEENQSPRSFOKKTTHYFLAVERLMDYGMSSSPHYLRN 1740  
QY 1740 RAQSGVPOEKVAVPOEPDQSFOTOLYRGELNHLGILGPYIRAEVEDNIMYFERMQAS 1799  
D 1741 RAQSGVPOEKVAVPOEPDQSFOTOLYRGELNHLGILGPYIRAEVEDNIMYFERMQAS 1800  
QY 1800 RPYSFYSSLISYEDDQOGAEBRKNFVKNETKYKVOHHMAFPKDEPCKMAVFS 1859  
D 1801 RPYSFYSSLISYEDDQOGAEBRKNFVKNETKYKVOHHMAFPKDEPCKMAVFS 1860  
QY 1860 VDLEKDVHSGILGPLVCHTNLNPANHQRQTVQOEFALFTTIFDETKSMYFTJEMNERNCR 1919  
D 1861 VDLEKDVHSGILGPLVCHTNLNPANHQRQTVQOEFALFTTIFDETKSMYFTJEMNERNCR 1920  
QY 1920 APCNIOEMDPTFKENRFEHAINGYIMDTLPOLVYVAAOQRTIRWYLLSMGNSNIHSHFSG 1979  
D 1921 APCNIOEMDPTFKENRFEHAINGYIMDTLPOLVYVAAOQRTIRWYLLSMGNSNIHSHFSG 1980  
QY 1980 HVFYVRRKKEEYKMAALNLYPGVETVENLPKAGIMRVECLGELHLAGMSTFLVYSNK 2039  
D 1981 HVFYVRRKKEEYKMAALNLYPGVETVENLPKAGIMRVECLGELHLAGMSTFLVYSNK 2040  
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D 2041 COTPLGMASSHINDFOITASGGYOGMAKRLRLHYSGSIAWASTKEPSWIKVDLAPMI 2100  
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D 2101 HGIKTQGAROKTSSLYISQFTIIMYSLDGKKWQYIRGNSGTILMPFGNVSSGIKRINIF 2160  
QY 2160 NPPIIARTIRLHPTHYSIRSTLRMELMCDLNSCMLPGESKASISDAQITASSYFTNMF 2219  
D 2161 NPPIIARTIRLHPTHYSIRSTLRMELMCDLNSCMLPGESKASISDAQITASSYFTNMF 2220  
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D 2221 ATWSPSKARHLHLOGRSANRPOVNNPKEMLOVDPOKTMKVTGVTTOGVKSLTSMYKEE 2280  
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D 2281 LISSQDGHQWTLFPONGKVKYPOGQDQSFPPVYVNSLDPPLLTRYLRIHPQSWHOIALR 2340  
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D 2341 MEVLGCEAODLY 2352  
RESULT 66  
AAW11345  
ID AAW11345 standard; Protein: 2352 AA.  
XX AAW11345;  
AC AAW11345;  
XX 17-NOV-1997 (first entry)  
XX



DE Active Factor VIII:C analogue residue 250 P insertion.  
XX  
KM Factor VIII:C analogue; glycoprotein; blood coagulation cascade;  
KM fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KM plasma protease; thrombin; immunogen; antibody; haemophilia; therapy;  
XX proteolytic cleavage.  
OS Homo sapiens.  
OS Synthetic.  
XX  
FH Key Location/Qualifiers  
FH Peptide 1..19  
FH /note= "signal peptide"  
FT Protein 20..2352  
FT /note= "mature Factor VIII:C"  
FT Region 20..1668  
FT /note= "heavy chain fragment"  
FT Misc-difference 270  
FT /note= "Inserted residue"  
FT Region 1669..2351  
FT /note= "light chain fragment"  
FT Domain 761..1668  
FT /note= "B domain"  
XX  
PN M09703195-A1.  
XX  
PD 30-JAN-1997.  
XX  
PF 09-JUL-1996; 96WO-US11444.  
XX  
PR 11-JUL-1995; 95US-0001025.  
XX  
PA (CHIR ) CHIRON CORP.  
XX  
PI Cohen FE, Hung DT, Innis M;  
XX WPI; 1997-119050/11.  
XX  
DR  
XX  
PT Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophilias, by improvement of  
PT haemostasis  
XX  
PS  
XX Claim 11: Page -: 90pp; English.  
XX  
CC AAM1330-w11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophilias, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX  
SQ Sequence 2352 AA;  
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;  
OY 1 M0E1STGCFCLLRFCFSATRRYYIGAVELSNQYMSDGLGELPVNARPPRPVPSFFPN 60  
|||||

DB 1 M0E1STGCFCLLRFCFSATRRYYIGAVELSNQYMSDGLGELPVNARPPRPVPSFFPN 60  
OY 61 TSVYVTKKTLFVEFEDLHFNARPRPPMGLGPTLOAEVDTVYITLKKMASHPSLSHAV 120  
|||||  
DB 61 TSVYVTKKTLFVEFEDLHFNARPRPPMGLGPTLOAEVDTVYITLKKMASHPSLSHAV 120  
OY 121 GVSYWKASEGAEYDDQTSOREKEDKVPFGSGSHTYVQVLEKNGPMASDPCLLTYSYLSH 180  
|||||  
DB 121 GVSYWKASEGAEYDDQTSOREKEDKVPFGSGSHTYVQVLEKNGPMASDPCLLTYSYLSH 180  
OY 181 VDLVYDNLKSGILGALVYCRGSLAKKQOTLHKFLLFAVFDGKSMSEFKNLSMDRD 240  
|||||  
DB 181 VDLVYDNLKSGILGALVYCRGSLAKKQOTLHKFLLFAVFDGKSMSEFKNLSMDRD 240  
OY 241 AASARAMPKHTTVNGVYNSLSRELIGCHIR-KSYVHWYIGCTTPEVNSFTLEGGTFVLRN 299  
|||||  
DB 241 AASARAMPKHTTVNGVYNSLSRELIGCHIR-KSYVHWYIGCTTPEVNSFTLEGGTFVLRN 299  
OY 300 HQQACDSLSPTTFLLTAOTLMDLGGFLFCHISSHODGMEAVYKVDSCPEBPOLRMKN 359  
|||||  
DB 301 HQQASLEISPTTFLLTAOTLMDLGGFLFCHISSHODGMEAVYKVDSCPEBPOLRMKN 360  
OY 360 EEAEDYDDDLTDSMDVYRFDNMSPSFTQIRSAKKHPTWVHTAAEEDMDAPLYL 419  
|||||  
DB 361 EEAEDYDDDLTDSMDVYRFDNMSPSFTQIRSAKKHPTWVHTAAEEDMDAPLYL 420  
OY 420 APDDRYSKSOYLNNGPQIRGRKRYKVMAYTDEFTFRTBAI0HESGILGLVGEVGT 479  
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|||||  
DB 481 LLTIIFKNQASRPYNIYHGITDVRPLYSRRLPKGVKHLKDFLLPELIFKYKWTYVEDG 540  
OY 540 PTKSDPCLTTRYSSFPVNMERDLASGLIPLLTICKSVQORNOIMSKRVLLFSEVD 599  
|||||  
DB 541 PTKSDPCLTTRYSSFPVNMERDLASGLIPLLTICKSVQORNOIMSKRVLLFSEVD 600  
OY 600 ENRSYVLTENIQRFLLPNPAGVLEDBEFOASNMHSTNGVYEDSLQVSLCHEVAYWYL 659  
|||||  
DB 601 ENRSYVLTENIQRFLLPNPAGVLEDBEFOASNMHSTNGVYEDSLQVSLCHEVAYWYL 660  
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|||||  
DB 661 SIGAOTDFLSVFESGYFKHKWYEDTLTLPFSGEYVFMSMENPGLMILGCHNSDFRNR 720  
OY 720 GMTALLKXSGCDKMTG DYEDSYEDISAVILSKNNALEPFSQNSRHSPTKQOFNAT 779  
|||||  
DB 721 GMTALLKXSGCDKMTG DYEDSYEDISAVILSKNNALEPFSQNSRHSPTKQOFNAT 780  
OY 780 IPENDIERTDPEFAHRTPMK10NVSSDDLMLLRQSPFHGSLSLDQEAKEYTFSDP 839  
|||||  
DB 781 IPENDIERTDPEFAHRTPMK10NVSSDDLMLLRQSPFHGSLSLDQEAKEYTFSDP 840  
OY 840 SPGALDSNNSLSEMTTHRPOLHNSGMYETPESGLQRLNEKIGTTAAATELKKLDFKVS 899  
|||||  
DB 841 SPGALDSNNSLSEMTTHRPOLHNSGMYETPESGLQRLNEKIGTTAAATELKKLDFKVS 900  
OY 900 TSNNLITRTPSDNLAACDTSTSGRPSAPVHYOSDITLFEKKSPTLREGGSLISE 959  
|||||  
DB 901 TSNNLITRTPSDNLAACDTSTSGRPSAPVHYOSDITLFEKKSPTLREGGSLISE 960  
OY 960 ENNDSKLLSEGLMNSQSSGKNVSTSEGRLEFGKRAHGPALLTRKDNALFKVSIISLKT 1019  
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DB 961 ENNDSKLLSEGLMNSQSSGKNVSTSEGRLEFGKRAHGPALLTRKDNALFKVSIISLKT 1020  
OY 1020 NKTSNNSATNKRTHIDPSSLLENSPVQNTLESDFEKKVPLIHDHMLMDKNAATLR 1079  
|||||  
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|||||  
DB 1081 LNMNSKTTSSKNEMVQOKKEEPTIPAPQNDMSFKNMLFLEPSARW10RHGKNSLNS 1140

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 DB 1741 RAQSGSVPOFKVYFOEFTDGSFTQPLYRGELNHLGLCPYRAVEDNINWYTRNQS 1800  
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 DB 1801 RPYFSYSLISYEEDROGAEPKKNFVKNETKTYFKVQHMAPTKDEFDCKANAYPSD 1860  
 QY 1860 VDLEKDVHSLIGPLVCHRTNLTNPAHGRQYTVQEFALFTIDEKTSWYTFENNERCR 1919  
 DB 1861 VDLEKDVHSLIGPLVCHRTNLTNPAHGRQYTVQEFALFTIDEKTSWYTFENNERCR 1920  
 QY 1920 APCNIOMEDPTEKENYFHAINGYIMDTLPGLVMAODRIRWYLLSGNSNENIHSIHFSG 1979  
 DB 1921 APCNIOMEDPTEKENYFHAINGYIMDTLPGLVMAODRIRWYLLSGNSNENIHSIHFSG 1980  
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 DB 2101 IHCITQGAROKESSLYISOFIIMYSLDGKKQOTYRGSTTTLWVFGVNDSSGICKHNIF 2160  
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 DB 2221 ATWSBKAARLHLOGRSNANRPVNNPKEMLOVDQKTMKVTGVTGQVSKLTSKYKEF 2280  
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 DB 2281 LISSQDGHQWTLFFQNGKVKYFQGNQDSFTPVVNSLDPLRLRYLRHPOSWHQIALR 2340  
 QY 2340 MEVLGCEADOLY 2351  
 DB 2341 MEVLGCEADOLY 2352  
 RESULT 67  
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 AC 17-NOV-1997 (first entry)  
 DT 17-NOV-1997 (first entry)  
 XX Active Factor VIII:C analogue residue 249 F/E/P insertion.  
 DE Factor VIII:C: analogue: glycoprotein; blood coagulation cascade;  
 KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
 KW plasma protease; thrombin; immunogen; antibody; haemophilic therapy;  
 KW proteolytic cleavage.  
 OS Homo sapiens.  
 OS Synthetic.  
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 FT Modified-site  
 FT 268  
 FT /label= "Phe, Glu, Pro  
 FT /note= "inserted residue"  
 FT Region  
 FT 1659..2351  
 FT /note= "light chain fragment"  
 FT 761..1668  
 FT /note= "B domain"  
 FT Domain  
 PD M09703195-A1.  
 PD 30-JAN-1997.  
 PD 09-JUL-1996; 96MO-US11444.  
 PD 11-JUL-1995; 95DS-0001025.  
 PA (CHIR ) CHIRON CORP.  
 PI Cohen FE, Hung DT, Innis M;  
 DR WPI: 1997-119050/11.  
 XX Factor VIII:C analog modified adjacent to a non-activating Arg  
 PT residue - used in the treatment of haemophiliacs, by improvement of  
 PT haemostasis  
 PT Claim 12; Page -: 90pp; English.  
 XX AAM11350-W11472 represent active Factor VIII:C analogues of the  
 CC invention. These sequences were created by mutating the wild type Factor  
 CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
 CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
 CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
 CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
 CC participates in the blood coagulation cascade that ultimately converts

CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophiliacs, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.

XX Sequence 2352 AA:

Query Match 99.9% Score 12407.5; DB 18; Length 2352;

Best Local Similarity 100.0%; Pred. No. 0;

Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

QY 1 MOEISTCFELCLNFCPSATRRYYLGAVELSDMYQMSDGLPEVDARFPPRYKSPFN 60  
DB 1 MOEISTCFELCLNFCPSATRRYYLGAVELSDMYQMSDGLPEVDARFPPRYKSPFN 60  
QY 61 TSVYKKTLFEVETDHLFNIAKPRPMGLGPTIOAEVYDTVYITLKNASHPVSLHAY 120  
DB 61 TSVYKKTLFEVETDHLFNIAKPRPMGLGPTIOAEVYDTVYITLKNASHPVSLHAY 120  
QY 121 GVSYKASGAEYDQTSQREKEDKYFGGSHYVYQYLAENGPASDPLCTYSLSH 180  
DB 121 GVSYKASGAEYDQTSQREKEDKYFGGSHYVYQYLAENGPASDPLCTYSLSH 180  
QY 121 GVSYKASGAEYDQTSQREKEDKYFGGSHYVYQYLAENGPASDPLCTYSLSH 180  
DB 121 GVSYKASGAEYDQTSQREKEDKYFGGSHYVYQYLAENGPASDPLCTYSLSH 180  
QY 181 VDLVKDLSGLIGALLVCREGLAKETQTLNFKLFAVDEGKSWHSEKNSLMQDD 240  
DB 181 VDLVKDLSGLIGALLVCREGLAKETQTLNFKLFAVDEGKSWHSEKNSLMQDD 240  
QY 241 AASARAPKMTHTVNGYVNRSLPGLIGC-HRKSVMHVIGNGTTPVSHIFLEGHTFLVN 299  
DB 241 AASARAPKMTHTVNGYVNRSLPGLIGC-HRKSVMHVIGNGTTPVSHIFLEGHTFLVN 299  
QY 241 AASARAPKMTHTVNGYVNRSLPGLIGC-HRKSVMHVIGNGTTPVSHIFLEGHTFLVN 299  
DB 241 AASARAPKMTHTVNGYVNRSLPGLIGC-HRKSVMHVIGNGTTPVSHIFLEGHTFLVN 299  
QY 300 HROASLEISPTFLAOTLMDLQGLFLLFCHISSHOHOGMEAYYKVDSCPEEQLMKNN 359  
DB 300 HROASLEISPTFLAOTLMDLQGLFLLFCHISSHOHOGMEAYYKVDSCPEEQLMKNN 359  
QY 301 HROASLEISPTFLAOTLMDLQGLFLLFCHISSHOHOGMEAYYKVDSCPEEQLMKNN 360  
DB 301 HROASLEISPTFLAOTLMDLQGLFLLFCHISSHOHOGMEAYYKVDSCPEEQLMKNN 360  
QY 360 EEAEDYDDDLTJSEMDVVRFPDDNSPSFIQIRSVAKKHPKTVWHYIAAEEEDMDYAPVL 419  
DB 360 EEAEDYDDDLTJSEMDVVRFPDDNSPSFIQIRSVAKKHPKTVWHYIAAEEEDMDYAPVL 419  
QY 361 EEAEDYDDDLTJSEMDVVRFPDDNSPSFIQIRSVAKKHPKTVWHYIAAEEEDMDYAPVL 420  
DB 361 EEAEDYDDDLTJSEMDVVRFPDDNSPSFIQIRSVAKKHPKTVWHYIAAEEEDMDYAPVL 420  
QY 420 APDDRSYKSOYLINNGPQRIIGRKYKVFMAVYDEFTKTRREALQHSGLGLLYGEVGT 479  
DB 420 APDDRSYKSOYLINNGPQRIIGRKYKVFMAVYDEFTKTRREALQHSGLGLLYGEVGT 479  
QY 421 APDDRSYKSOYLINNGPQRIIGRKYKVFMAVYDEFTKTRREALQHSGLGLLYGEVGT 480  
DB 421 APDDRSYKSOYLINNGPQRIIGRKYKVFMAVYDEFTKTRREALQHSGLGLLYGEVGT 480  
QY 480 LLIIFKNOASRPYNTYPHGIDVAPLYSRRLPKGVAKHLKDFPLPGLIFKTKVTVVEDG 539  
DB 480 LLIIFKNOASRPYNTYPHGIDVAPLYSRRLPKGVAKHLKDFPLPGLIFKTKVTVVEDG 539  
QY 481 LLIIFKNOASRPYNTYPHGIDVAPLYSRRLPKGVAKHLKDFPLPGLIFKTKVTVVEDG 540  
DB 481 LLIIFKNOASRPYNTYPHGIDVAPLYSRRLPKGVAKHLKDFPLPGLIFKTKVTVVEDG 540  
QY 540 PTKSDPRCLTRYSSYFVMERDLASGLIGPLLCYKESYVDGONGIMSDRNYLTSVSD 599  
DB 540 PTKSDPRCLTRYSSYFVMERDLASGLIGPLLCYKESYVDGONGIMSDRNYLTSVSD 599  
QY 541 PTKSDPRCLTRYSSYFVMERDLASGLIGPLLCYKESYVDGONGIMSDRNYLTSVSD 600  
DB 541 PTKSDPRCLTRYSSYFVMERDLASGLIGPLLCYKESYVDGONGIMSDRNYLTSVSD 600  
QY 600 ENNSWTLTENIDRFLPNPAGVQLEDPEFOASNTMHSINGYVDSIQSLCYLHEVATWYL 659  
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QY 601 ENNSWTLTENIDRFLPNPAGVQLEDPEFOASNTMHSINGYVDSIQSLCYLHEVATWYL 660  
DB 601 ENNSWTLTENIDRFLPNPAGVQLEDPEFOASNTMHSINGYVDSIQSLCYLHEVATWYL 660  
QY 660 SIGAOTDPLSVFSGYTKHKMYEDTLTLPFSGSETVMENGLMILGCHNSPFRNR 719  
DB 660 SIGAOTDPLSVFSGYTKHKMYEDTLTLPFSGSETVMENGLMILGCHNSPFRNR 719  
QY 661 SIGAOTDPLSVFSGYTKHKMYEDTLTLPFSGSETVMENGLMILGCHNSPFRNR 720  
DB 661 SIGAOTDPLSVFSGYTKHKMYEDTLTLPFSGSETVMENGLMILGCHNSPFRNR 720  
QY 720 GMTALKVSSCDKNQGDYEDYEDISAYLLSNNAIPERSOSNRPSRROKORNAAT 779  
DB 720 GMTALKVSSCDKNQGDYEDYEDISAYLLSNNAIPERSOSNRPSRROKORNAAT 779  
QY 721 GMTALKVSSCDKNQGDYEDYEDISAYLLSNNAIPERSOSNRPSRROKORNAAT 780  
DB 721 GMTALKVSSCDKNQGDYEDYEDISAYLLSNNAIPERSOSNRPSRROKORNAAT 780  
QY 780 IPENDIEKTDPMFAHRTPMKIQONVSSDMLMLROSPTPHGLSLSDLOEAKYETESDDP 839  
DB 780 IPENDIEKTDPMFAHRTPMKIQONVSSDMLMLROSPTPHGLSLSDLOEAKYETESDDP 839

DB 781 IPENDIEKTDPMFAHRTPMKIQONVSSDMLMLROSPTPHGLSLSDLOEAKYETESDDP 840  
QY 840 SPGATISNNSLEMTNFRPOLHSGDWVFPESGLOLRNKEKGTATATELKLIDPKVSS 899  
DB 841 SPGATISNNSLEMTNFRPOLHSGDWVFPESGLOLRNKEKGTATATELKLIDPKVSS 900  
QY 900 TSNNLISTIPSONLAAGTDNTSSLGPPSMYVHTDSOLDTTLFGKSSPFLPESGPILSSE 959  
DB 901 TSNNLISTIPSONLAAGTDNTSSLGPPSMYVHTDSOLDTTLFGKSSPFLPESGPILSSE 960  
QY 960 ENNDSKLTESGLMNSOESSMCKNVSTESGRLEKGRAPALTLKONALFKYSILKT 1019  
DB 961 ENNDSKLTESGLMNSOESSMCKNVSTESGRLEKGRAPALTLKONALFKYSILKT 1020  
QY 1020 NKTSSNATNKRKTHIDGSLILNEMSPVWONILSEPTFEKKTPLIDRMLMKNATAR 1079  
DB 1021 NKTSSNATNKRKTHIDGSLILNEMSPVWONILSEPTFEKKTPLIDRMLMKNATAR 1080  
QY 1080 LNMHNSKTTSSKNMEMVOQKKEGPIPPDAONPDMSPFKMLFPESARWIORTHGKNSLNS 1139  
DB 1081 LNMHNSKTTSSKNMEMVOQKKEGPIPPDAONPDMSPFKMLFPESARWIORTHGKNSLNS 1140  
QY 1140 GGGSPKOLVSLGPEKSYEGONFLSEKKNVYVKGGEFTDVLKEMVPSRRNLFNLND 1199  
DB 1141 GGGSPKOLVSLGPEKSYEGONFLSEKKNVYVKGGEFTDVLKEMVPSRRNLFNLND 1200  
QY 1200 NLHENNTNHOEKKIOBEIEKKEETLQENYVLPQIRHTVGTKNFKNLPFLSTQONVEGSY 1259  
DB 1201 NLHENNTNHOEKKIOBEIEKKEETLQENYVLPQIRHTVGTKNFKNLPFLSTQONVEGSY 1260  
QY 1260 DGAYAPVADFRSLNDSTNRTKKTATFHSKGEENLEGLNQTQOYEVYACTRISPN 1319  
DB 1261 DGAYAPVADFRSLNDSTNRTKKTATFHSKGEENLEGLNQTQOYEVYACTRISPN 1320  
QY 1320 TSOQNFVTOQSKRALKOPFLPLEETLEKELIYDDSTQWMSKNMHLPSLQIDVNEK 1379  
DB 1321 TSOQNFVTOQSKRALKOPFLPLEETLEKELIYDDSTQWMSKNMHLPSLQIDVNEK 1380  
QY 1380 EKGATQSPSLDCTLRSHSIPQANRSPPLAKVSSPSTRIYTLRVLFDONSSHLPAS 1439  
DB 1381 EKGATQSPSLDCTLRSHSIPQANRSPPLAKVSSPSTRIYTLRVLFDONSSHLPAS 1440  
QY 1440 YRKDQSGVQSSHFLQGAKKNNLSLALTLLEMTGDOREVSGIGTSATNSVYKKVENTVL 1499  
DB 1441 YRKDQSGVQSSHFLQGAKKNNLSLALTLLEMTGDOREVSGIGTSATNSVYKKVENTVL 1500  
QY 1500 PKPDLPTSGKVELLPKYHIYOKDLPETNSGPGHLDLVGSLQGTGATKYNBAR 1559  
DB 1501 PKPDLPTSGKVELLPKYHIYOKDLPETNSGPGHLDLVGSLQGTGATKYNBAR 1560  
QY 1560 PGKVPFLRVATESSAKTPSKLLDPLANDNHGTQIPEKEMKSOEKSPEKTAFFKKDITIS 1619  
DB 1561 PGKVPFLRVATESSAKTPSKLLDPLANDNHGTQIPEKEMKSOEKSPEKTAFFKKDITIS 1620  
QY 1620 LNCESNHAIALINBQNKPELEVTMAKOGRTBRLCSQRPVLAKHQNEIRTTLOSDE 1679  
DB 1621 LNCESNHAIALINBQNKPELEVTMAKOGRTBRLCSQRPVLAKHQNEIRTTLOSDE 1680  
QY 1680 EIDYDGTIYEMKKEEDFDYDEDENOBSPFOKKTATHTYIAAVERLMQYKSSSPHYLRN 1739  
DB 1681 EIDYDGTIYEMKKEEDFDYDEDENOBSPFOKKTATHTYIAAVERLMQYKSSSPHYLRN 1740  
QY 1740 RAQSGVPOFKKVFQEFIDGSEFTQPLRYGBLBNHGLGPIYRAVEDNIMVYFRNOAS 1799  
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QY 1800 RPYSFYSLSIYVEEOGAGPBRKNFYKPEKTYKWKQONHMAATKQEFCKMAVFSO 1859  
DB 1801 RPYSFYSLSIYVEEOGAGPBRKNFYKPEKTYKWKQONHMAATKQEFCKMAVFSO 1860  
QY 1860 VDLKDVHSLGIPPLVCHTNTLPNAGROYVQOEBALFTTIEDTCKSWYETEMENCR 1919  
DB 1860 VDLKDVHSLGIPPLVCHTNTLPNAGROYVQOEBALFTTIEDTCKSWYETEMENCR 1919

DB 1861 VDLEKDVHSGILGIPLVCHTNTLNPAHQRYTQEFALFTIEDTKSWFTENNERNCR 1920  
QY 1920 APCNIQMEDPTEKENTREHAINGYIMDTLPGLVVAOQRIKMTLSMGSNENIHSIHSG 1979  
DB 1921 APCNIQMEDPTEKENTREHAINGYIMDTLPGLVVAOQRIKMTLSMGSNENIHSIHSG 1980  
QY 1980 HFTVYRKKEEKYKALNLYPGVFETVEMLPKAGIMVEECLIGEHLMAGMSTLFLVYSNK 2039  
DB 1981 HFTVYRKKEEKYKALNLYPGVFETVEMLPKAGIMVEECLIGEHLMAGMSTLFLVYSNK 2040  
QY 2040 CQTPGLMASGHIRPQTASGOYQOMAPKRLAHYSGSINAMSTKEPSEMITVDLAPMI 2099  
DB 2041 CQTPGLMASGHIRPQTASGOYQOMAPKRLAHYSGSINAMSTKEPSEMITVDLAPMI 2100  
QY 2100 IHGKTQAGROKFSSTLYISOFTIMTSLDGKKWQYTRGNSGTGLMVFEGVNDSSGIRKHNIF 2159  
DB 2101 IHGKTQAGROKFSSTLYISOFTIMTSLDGKKWQYTRGNSGTGLMVFEGVNDSSGIRKHNIF 2160  
QY 2160 NPIIARIYRIHPHYSIRSTLMELMGCDLNSGMPLEMSKASIDAOITASSYFTNMF 2219  
DB 2161 NPIIARIYRIHPHYSIRSTLMELMGCDLNSGMPLEMSKASIDAOITASSYFTNMF 2220  
QY 2220 ATWSPSKARLHLQGRSNAMPQVNNKEMWLYDEQKTKWYGTQGVKSLTSMYKEF 2279  
DB 2221 ATWSPSKARLHLQGRSNAMPQVNNKEMWLYDEQKTKWYGTQGVKSLTSMYKEF 2280  
QY 2280 LISSODGHQWTLFPONGKVKYFGQMODSFTPPVNSLDPLLTFRYLRIHPQSWHQIALR 2339  
DB 2281 LISSODGHQWTLFPONGKVKYFGQMODSFTPPVNSLDPLLTFRYLRIHPQSWHQIALR 2340  
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DB 2341 MEVLGCEADOLY 2352

RESULT 68  
AAM1353  
ID AAM1353 standard. Protein: 2352 AA.  
AC AAM1353;  
DT 17-NOV-1997 (first entry)  
DE Active Factor VIII:C analogue residue 279 P insertion.  
XX Factor VIII:C analogue; glycoprotein; blood coagulation cascade;  
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KM plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;  
KM proteolytic cleavage.  
XX Homo sapiens.  
OS Synthetic.  
XX Key Location/Qualifiers  
FH Peptide 1..19  
FT /note= "signal peptide"  
FT Protein 20..2352  
FT /note= "mature Factor VIII:C"  
FT Region 20..1668  
FT /note= "heavy chain fragment"  
FT MISC-difference 298  
FT /note= "inserted residue"  
FT Region 1669..2351  
FT /note= "light chain fragment"  
FT Domain 761..1668  
FT /note= "B domain"  
XX MO9703195-A1.  
XX 30-JAN-1997.  
XX 09-JUL-1996; 96MO-US11444..

PR 11-JUL-1995; 95US-0001025.  
XX (CHIR ) CHIRON CORP.  
XX Cohen FE, Hung DT, Innis M;  
PI WPI: 1997-119050/11.  
XX Factor VIII:C analog modified adjacent to a non-activating Arg  
PR residue - used in the treatment of haemophilias, by improvement of  
PR haemostasis  
XX Claim 13; Page -: 90pp; English.  
XX AAM1330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophilias, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX Sequence 2352 AA:  
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;  
QY 1 MOITLSCFPLICLLRPFCSATRRYIAGVELSMDYQMSDGLPYDARPPRRVKSPPFN 60  
DB 1 MOITLSCFPLICLLRPFCSATRRYIAGVELSMDYQMSDGLPYDARPPRRVKSPPFN 60  
QY 61 TSVYKKTLEVEETDHLNIAKRPWMGLGPTIOAEYDVTYITLKMASSHVSLHAY 120  
DB 61 TSVYKKTLEVEETDHLNIAKRPWMGLGPTIOAEYDVTYITLKMASSHVSLHAY 120  
QY 121 GSVYWKASGEAEDDOTSOREKEDKVPFGSGSHYVQVLEKNGPMASDPCLCTLYSLSH 180  
DB 121 GSVYWKASGEAEDDOTSOREKEDKVPFGSGSHYVQVLEKNGPMASDPCLCTLYSLSH 180  
QY 181 VDLVKDNLNSGILGALLVREGSLAKETQTLAKTLLFAVFDEGKMSHETKNSLMODRD 240  
DB 181 VDLVKDNLNSGILGALLVREGSLAKETQTLAKTLLFAVFDEGKMSHETKNSLMODRD 240  
QY 241 AASARAMPKHTVNGVYNSRLGLIGCRKRSVYVHWVIGMTPTREVSIFLEGHFLY- RN 299  
DB 241 AASARAMPKHTVNGVYNSRLGLIGCRKRSVYVHWVIGMTPTREVSIFLEGHFLY- RN 299  
QY 300 HROQSLSEISPTTFLAQTLLMDLQGLFLCHTSSHDQMEALVYKVDSCREPPOLRMKN 359  
DB 301 HROQSLSEISPTTFLAQTLLMDLQGLFLCHTSSHDQMEALVYKVDSCREPPOLRMKN 360  
QY 360 BEAEDYDDDLTDSQEMVYRFPDDNSPFIQIRSAVAKKHPKTWVHYIAAEEEDMDYAPLV 419  
DB 361 BEAEDYDDDLTDSQEMVYRFPDDNSPFIQIRSAVAKKHPKTWVHYIAAEEEDMDYAPLV 420  
QY 420 APDRSYKSGYLLNNGPQIRGKRYKRYPMATTDFTFKTRALIOHESGILGLLYGEVGT 479  
DB 421 APDRSYKSGYLLNNGPQIRGKRYKRYPMATTDFTFKTRALIOHESGILGLLYGEVGT 480

Qy 480 LLIIFKNOASRPYNIYPHGITDVPRLYRRLPKCYKHLKDPILRLGELIFKKYNTVYEDS 539  
|||||  
Db 481 LLIIFKNOASRPYNIYPHGITDVPRLYRRLPKCYKHLKDPILRLGELIFKKYNTVYEDS 540  
|||||  
Qy 540 PTKSDPRLCTRYYSFVFNMERDLASGLIGPLLICYSVDORONOIMSDKRNVLTFESVD 599  
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Db 541 PTKSDPRLCTRYYSFVFNMERDLASGLIGPLLICYSVDORONOIMSDKRNVLTFESVD 600  
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Db 601 EKRSWYLTENIORFLPNPAGVQLEDPFQASINMHSINGVPSLOLSVCJHEVAAYYIL 660  
|||||  
Qy 660 SIGAQDTPLSVFSSGTFEKKMYEDTTLTFPSGGEYFVMSMENGWILICCHNSDRNR 719  
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Db 661 SIGAQDTPLSVFSSGTFEKKMYEDTTLTFPSGGEYFVMSMENGWILICCHNSDRNR 720  
|||||  
Qy 720 GMTALLKVSQDKNTGDYEDSYEDISAYLLSKNNALEPRFSFONSRRPSTROKOFNATY 779  
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Db 721 GMTALLKVSQDKNTGDYEDSYEDISAYLLSKNNALEPRFSFONSRRPSTROKOFNATY 780  
|||||  
Qy 780 IPENDIEKTPWFPAHRTPMPKIQNVSSDMLMLKQSPTRHGLSLSDLOEAKYETFSDDP 839  
|||||  
Db 781 IPENDIEKTPWFPAHRTPMPKIQNVSSDMLMLKQSPTRHGLSLSDLOEAKYETFSDDP 840  
|||||  
Qy 840 SPGATDSNNSLSEMTFRPOLHSGDMYFPESGLOLRMEKLGTTAATELKIDEPYSS 899  
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Db 841 SPGATDSNNSLSEMTFRPOLHSGDMYFPESGLOLRMEKLGTTAATELKIDEPYSS 900  
|||||  
Qy 900 TSNNLITIPSDNLAAGTNTSSLCGPPMPVHYDSQDITTLFEGKSSPLTESGGPLSLSE 959  
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Db 901 TSNNLITIPSDNLAAGTNTSSLCGPPMPVHYDSQDITTLFEGKSSPLTESGGPLSLSE 960  
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Qy 960 ENNDKSLLESGIMNSOESSMGKNVSTESGRLFGKRAHGPALTRFDNALFKVYSISLTKT 1019  
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Db 961 ENNDKSLLESGIMNSOESSMGKNVSTESGRLFGKRAHGPALTRFDNALFKVYSISLTKT 1020  
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Qy 1020 NKTSNNSATNKTTHIDGSPILLIENSPLYWONILESDPEFKKTPPLIHRMIMDKNAALR 1079  
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Db 1021 NKTSNNSATNKTTHIDGSPILLIENSPLYWONILESDPEFKKTPPLIHRMIMDKNAALR 1080  
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Qy 1080 LNMHSNKTSSKNMEVQOKEGPITPDQONPDMSFFKMLFJPESARWIOPTHGKNSLNS 1139  
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Db 1081 LNMHSNKTSSKNMEVQOKEGPITPDQONPDMSFFKMLFJPESARWIOPTHGKNSLNS 1140  
|||||  
Qy 1140 GGGSPKOLVSLGPEKSVEGONFLSEKNKVVVGGEFTKDVGLKEVFPSSRNILFLNL 1199  
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|||||  
Qy 1260 DGAIVAPVLQDFRSLNDSTNRKKTAAHFSKGEEBENLEGLGNOTKOIYEKTACTTRISPN 1319  
|||||  
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Db 1321 TSOQNFVYORSKRALKQFLPLEETELEKRIIVDTSTOWSKNMKHLPESTLTOIDYNEK 1380  
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Qy 1380 EKGATOSPISDCITRSHSIPQANSPLPIKAVSSPSTIPYILPVPVLPONSSSHLPAAS 1439  
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Db 1381 EKGATOSPISDCITRSHSIPQANSPLPIKAVSSPSTIPYILPVPVLPONSSSHLPAAS 1440  
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Qy 1440 YRKDSGOESSHFLQGAKKNNLSAAILLEMTGDOREVSGIGTSATNSVYKKVENTVL 1499  
|||||  
Db 1441 YRKDSGOESSHFLQGAKKNNLSAAILLEMTGDOREVSGIGTSATNSVYKKVENTVL 1500  
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Qy 1500 PKPDLPTSGVELLPVNIYOKDLFPTETSGNSPGHLDLVEGSLLOGEGAIKMNANR 1559  
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Db 1501 PKPDLPTSGVELLPVNIYOKDLFPTETSGNSPGHLDLVEGSLLOGEGAIKMNANR 1560  
|||||  
Qy 1560 PKGVPEFLVATRESSAKIPSKLDPPLAMDNHGTGPIREBEMKSOEKSPEKTAFAKKKDTILS 1619  
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Db 1561 PKGVPEFLVATRESSAKIPSKLDPPLAMDNHGTGPIREBEMKSOEKSPEKTAFAKKKDTILS 1620  
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Qy 1620 LMACESNHAIATAINEGQKPEIEVYMAKOGRTBRLCSQNPVLKRRHOREITRTTLQSDOE 1679  
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Db 1621 LMACESNHAIATAINEGQKPEIEVYMAKOGRTBRLCSQNPVLKRRHOREITRTTLQSDOE 1680  
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Qy 1680 EIDYDPTISYEMKKEDEFDIYEDENQSPRSFOKTRHRYFAVERLMDYQSSSPVLRN 1739  
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Db 1681 EIDYDPTISYEMKKEDEFDIYEDENQSPRSFOKTRHRYFAVERLMDYQSSSPVLRN 1740  
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Qy 1740 RAQSGSVQKRYVROEPLDGSFPOTPLRBELENHGLGPIYRAVEDNIMTFERNQAS 1799  
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Db 1741 RAQSGSVQKRYVROEPLDGSFPOTPLRBELENHGLGPIYRAVEDNIMTFERNQAS 1800  
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Qy 1800 RPYSFYSLSIYEBEODROGAEBRKNFYKPNETTYTFWKVOHNAFTKDEPDCKAMAFSD 1859  
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Db 1801 RPYSFYSLSIYEBEODROGAEBRKNFYKPNETTYTFWKVOHNAFTKDEPDCKAMAFSD 1860  
|||||  
Qy 1860 VDLKDVHSGLIGPLLVCHTNTLPNAGROVTVQEFALPFTTFDETKSWYFTEMERNCR 1919  
|||||  
Db 1861 VDLKDVHSGLIGPLLVCHTNTLPNAGROVTVQEFALPFTTFDETKSWYFTEMERNCR 1920  
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Qy 1920 APCNIOMEDPTFEKENRFRPAINGYIMDTLPGIYMAODORIIMYLLSMGSNENHSHIFSG 1979  
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Db 1921 APCNIOMEDPTFEKENRFRPAINGYIMDTLPGIYMAODORIIMYLLSMGSNENHSHIFSG 1980  
|||||  
Qy 1980 HFTVVRKKEEYKALYNLYPGVFETVEKLDPSKAGINRVBCLIGEHLAGMSTLEFLYYSNK 2039  
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Db 1981 HFTVVRKKEEYKALYNLYPGVFETVEKLDPSKAGINRVBCLIGEHLAGMSTLEFLYYSNK 2040  
|||||  
Qy 2040 CQTPFGNASGHIDFQITFASQYQGMAPKLARLHSGSINANSTKEPFSWIKYDILLAPMI 2099  
|||||  
Db 2041 CQTPFGNASGHIDFQITFASQYQGMAPKLARLHSGSINANSTKEPFSWIKYDILLAPMI 2100  
|||||  
Qy 2100 IHGKITOGAKOKFSSLYTSQFIIMYSLDGKKMOTYGCNSTGTLMFERNQSSGIXHNIF 2159  
|||||  
Db 2101 IHGKITOGAKOKFSSLYTSQFIIMYSLDGKKMOTYGCNSTGTLMFERNQSSGIXHNIF 2160  
|||||  
Qy 2160 NPPIIARYIRLAPRTHYSIRSTLRMELMCCDINSCNPLMESKASISDAQTASSYFTNMF 2219  
|||||  
Db 2161 NPPIIARYIRLAPRTHYSIRSTLRMELMCCDINSCNPLMESKASISDAQTASSYFTNMF 2220  
|||||  
Qy 2220 ATWSPSKARLHLQGRSNAMARPQVNNPKFEMLDQVDFOKTMYVTGTVQYKSLTSMYKKE 2279  
|||||  
Db 2221 ATWSPSKARLHLQGRSNAMARPQVNNPKFEMLDQVDFOKTMYVTGTVQYKSLTSMYKKE 2280  
|||||  
Qy 2280 LISSODGHOMTLEFRONGKVVYFQGNQDSFTPVVNSLDLPLLTRLRTHIPQSWYHOIAIR 2339  
|||||  
Db 2281 LISSODGHOMTLEFRONGKVVYFQGNQDSFTPVVNSLDLPLLTRLRTHIPQSWYHOIAIR 2340  
|||||  
Qy 2340 MEVLGCEADOLY 2351  
|||||  
Db 2341 MEVLGCEADOLY 2352  
|||||  
RESULT 69  
AAW11354  
ID AAW11354 standard; Protein: 2352 AA.  
XX  
AC AAW11354:  
DT 17-NOV-1997 (first entry)  
XX  
DE Active Factor VIII:C analogue residue 280 p insertion.  
XX  
KW Factor VIII:C analogue; glycoprotein; blood coagulation cascade;  
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KW plasma protease; thrombin; immunogen; antibody; haemophilias; therapy;  
KW proteolytic cleavage.  
OS Homo sapiens.  
OS Synthetic.

XX Key Location/Qualifiers  
FH Peptide 1..19  
FT /note="signal peptide"  
FT Protein 20..2352  
FT Region /note="mature Factor VIII:C"  
FT 20..1668  
FT /note="heavy chain fragment"  
FT Misc-difference 239  
FT /note="inserted residue"  
FT Region 1669..2351  
FT /note="light chain fragment"  
FT Domain 761..1668  
FT /note="b domain"  
PN MO9703195-A1.  
PD 30-JAN-1997.  
XX  
XX 09-JUL-1996; 96MO-US11444.  
XX  
XX 11-JUL-1995; 95US-0001025.  
XX  
XX (CHIR ) CHIRON CORP.  
XX  
XX Cohen FE, Hung DT, Innis M;  
PI WPI: 1997-119050/11.  
XX  
XX Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophilia, by improvement of  
PT haemostasis  
XX  
XX Claim 13; Page -: 90pp; English.  
XX  
XX AAM1330-M1472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophilia, by  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX  
SQ Sequence 2352 AA:  
Query Match 99.9%; Score 12407.5; DB 18; length 2352;  
Best local similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;  
QY 1 MOELSTCFPLCLARCFSATRRYIAGVELSDMYWOSDLGELPYDARFPPRYKSPFN 60  
DB 1 MOELSTCFPLCLARCFSATRRYIAGVELSDMYWOSDLGELPYDARFPPRYKSPFN 60  
QY 61 TSVYKKTLFVEFTDHLFNIAKPRPMWGLLPTIOAEVYDTVTTLKNMASHPSLHAY 120  
DB 61 TSVYKKTLFVEFTDHLFNIAKPRPMWGLLPTIOAEVYDTVTTLKNMASHPSLHAY 120  
QY 121 GVSYWKASGAEYDDOTSOREKEDKVPKGSHTYVWVLAKENGMAADPLCTLYSTLSH 180  
DB 121 GVSYWKASGAEYDDOTSOREKEDKVPKGSHTYVWVLAKENGMAADPLCTLYSTLSH 180

QY 181 VDLVKDNLNSGLIGALLVCRGSLAKERTQTLHKFILLFAVDEBKSWMHSETKNSLMODRD 240  
DB 181 VDLVKDNLNSGLIGALLVCRGSLAKERTQTLHKFILLFAVDEBKSWMHSETKNSLMODRD 240  
QY 241 AASARAMPKMTVNGVNRSLPGLICGHRKSVYWHYIGMTTPPVSHIFLEGHTFLVR-N 299  
DB 241 AASARAMPKMTVNGVNRSLPGLICGHRKSVYWHYIGMTTPPVSHIFLEGHTFLVR-N 300  
QY 300 HROASLEISPTIFPLFASGLMDLQPLIFCHISHOHOMENAYKVDSCPEEQLMKKN 359  
DB 301 HROASLEISPTIFPLFASGLMDLQPLIFCHISHOHOMENAYKVDSCPEEQLMKKN 360  
QY 360 EEAEDYDDDLTSEMDVYRFDDNSPFIQIRSVAKKHPTWVHYIAEEDMDVAPLVL 419  
DB 361 EEAEDYDDDLTSEMDVYRFDDNSPFIQIRSVAKKHPTWVHYIAEEDMDVAPLVL 420  
QY 420 APDRRSYKSOYLNNGPDRIGRKYKRFMAVTEPFKTRREALIOHESGILGFLYGFVGT 479  
DB 421 APDRRSYKSOYLNNGPDRIGRKYKRFMAVTEPFKTRREALIOHESGILGFLYGFVGT 480  
QY 480 LLITFKNQASRPYNTIPGCTIDVRLPLSRPKGVKHLKDPPIIPGEIFPKYKVTVEEG 539  
DB 481 LLITFKNQASRPYNTIPGCTIDVRLPLSRPKGVKHLKDPPIIPGEIFPKYKVTVEEG 540  
QY 540 PTKSDPCLTRRYSSFVAMERDLASGLIGPLICYKESVDQRGNOIMSDRNYILFSVD 599  
DB 541 PTKSDPCLTRRYSSFVAMERDLASGLIGPLICYKESVDQRGNOIMSDRNYILFSVD 600  
QY 600 ENBSWYITENIRPLPNPAGVOLDEPEFQASNTMHSINCYFDSLOLSTGLHVAWYTL 659  
DB 601 ENBSWYITENIRPLPNPAGVOLDEPEFQASNTMHSINCYFDSLOLSTGLHVAWYTL 660  
QY 660 SIGAQIDFLSVFPGSGYTKHKMYEDTLTLPFSGEYPMSENPGMLIGCNSDFRNR 719  
DB 661 SIGAQIDFLSVFPGSGYTKHKMYEDTLTLPFSGEYPMSENPGMLIGCNSDFRNR 720  
QY 720 GMTALLKVSCKDNTGDEYEDYSIDASYLLSKNNAIEFRSPONSRRPSTROKOPNAT 779  
DB 721 GMTALLKVSCKDNTGDEYEDYSIDASYLLSKNNAIEFRSPONSRRPSTROKOPNAT 780  
QY 780 IPEMDIKTPMPFAHRTMPKTIOWVSSDILMLRSPPHLSISDLOAKKETEESDOP 839  
DB 781 IPEMDIKTPMPFAHRTMPKTIOWVSSDILMLRSPPHLSISDLOAKKETEESDOP 840  
QY 840 SPGAIDSNNLSLMTFRPOLHSGDWFTPEBGLQRLNEXLGTATATLKRDLDFKYS 899  
DB 841 SPGAIDSNNLSLMTFRPOLHSGDWFTPEBGLQRLNEXLGTATATLKRDLDFKYS 900  
QY 900 TSNNLISTIPSDNLAAGTDNSTSLGPPSMFVHYDSOLDTTLFGKKSPLTESGGPLSLSE 959  
DB 901 TSNNLISTIPSDNLAAGTDNSTSLGPPSMFVHYDSOLDTTLFGKKSPLTESGGPLSLSE 960  
QY 960 ENNSKTLLEGSLMNSOESWGNKNTSPESGRLEKGRAGPALTLKONALFKYSISLMT 1019  
DB 961 ENNSKTLLEGSLMNSOESWGNKNTSPESGRLEKGRAGPALTLKONALFKYSISLMT 1020  
QY 1020 NKTSSNNSATNRKTHIDGSLLENSPSVWONILLESDFEKKVTLPIHDRMLAKNATLR 1079  
DB 1021 NKTSSNNSATNRKTHIDGSLLENSPSVWONILLESDFEKKVTLPIHDRMLAKNATLR 1080  
QY 1080 LNHMSNKTSSKMMEWQOKKEGPIPPDAONPMSFFKMLFESASRIORTGKKSLSNS 1139  
DB 1081 LNHMSNKTSSKMMEWQOKKEGPIPPDAONPMSFFKMLFESASRIORTGKKSLSNS 1140  
QY 1140 GGGSPKQVLVSLAPEKSVBGNFTSEKNKYVVGKGFTHKDGLEKXVPSSRLPLTIND 1199  
DB 1141 GGGSPKQVLVSLAPEKSVBGNFTSEKNKYVVGKGFTHKDGLEKXVPSSRLPLTIND 1200  
QY 1200 NLHENNTNHQEKKIOEIELEKRETLIOENNVLPQIHTVYGTNFKMKNLFLSTRONEGYS 1259  
DB 1201 NLHENNTNHQEKKIOEIELEKRETLIOENNVLPQIHTVYGTNFKMKNLFLSTRONEGYS 1260

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OY 1260 DGAYAVLQDFRSLNDSTNRTKHTAFSKGKEENLEGLOTKQIYEVACTRISPN 1319
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OY 1320 TSGQNFVQRSKRALQKQRLPLETELEKRIIVDQTSQNSKNNKHTPSTLQIDYNK 1379
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DB 1321 TSGQNFVQRSKRALQKQRLPLETELEKRIIVDQTSQNSKNNKHTPSTLQIDYNK 1380
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DB 1381 EKGAITQSPDCLTRSHSIPQANRSPDLIAVSSFPSIRPIYLTVLFQDNSSHLPAAS 1440
OY 1440 YRKDGQVQESHFFLOGKKNKSLAILTEPMQOREVSLGTSATNSYTKKVENTVL 1499
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DB 1441 YRKDGQVQESHFFLOGKKNKSLAILTEPMQOREVSLGTSATNSYTKKVENTVL 1500
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DB 1501 PKPDLPTSGKVELLPKHVIYQKDLPTETSNQSGHLDLYGSLDGTGAIKMEANR 1560
OY 1560 PKGVPLRAVATESSAKTPSKLLDPLAMDNHYGTQIPEKEMKSOEKSPKTAFFKKDTILS 1619
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DB 1561 PKGVPLRAVATESSAKTPSKLLDPLAMDNHYGTQIPEKEMKSOEKSPKTAFFKKDTILS 1620
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OY 1740 RAQGSVPOFKKVVQEQETDGSFTQPIYRCELNEHGLGIPYIRAEVDNIMTFNQAS 1799
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OY 1860 VDLEKDVHSGLIQPLLVCHTNLPNAHROVYQVEAFETTFDETKSWYFTENMRNCR 1919
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DB 1861 VDLEKDVHSGLIQPLLVCHTNLPNAHROVYQVEAFETTFDETKSWYFTENMRNCR 1920
OY 1920 APCNIQMEDPTFKENYRPHAINGYIMDTLPGVMAQDORIRVYLLSNGSMENHSHIFSG 1979
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DB 1981 HVEFTVAKKEEYKMAIYNLYPGVETVEMLEPSKAGIMRVECLIGELHAGMSTLELVYSNK 2040
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    |||||||
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DB 2101 IHGIKTOGAROKFSSLYISQFTIMYSIDGKKQNTYNGNSTGTLWAFNGNDSSGITHNF 2160
OY 2160 NPPIIARYIRLPHYYSIRSTLRMLNGLCDLNSCMLPGLMESKALSDAQITASSYFTNNF 2219
    |||||||
DB 2161 NPPIIARYIRLPHYYSIRSTLRMLNGLCDLNSCMLPGLMESKALSDAQITASSYFTNNF 2220
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OY 2280 LISSSDGHWMTLFFQNKVAVFQGNODSTFPVNSLDPPLTRILKRLHQSWHQAIALR 2339
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DB 2281 LISSSDGHWMTLFFQNKVAVFQGNODSTFPVNSLDPPLTRILKRLHQSWHQAIALR 2340
OY 2340 MEVLGCEADLY 2351

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DB 2341 MEVLGCEADLY 2352
    |||||||
RESULT 70
AAW11330
ID AAW11330 standard; Protein; 2352 AA.
XX
AAW11330;
AC 17-NOV-1997 (first entry)
DT
XX
Active Factor VIII:C analogue residue 218 F/E/P insertion.
XX
DE Factor VIII:C; analogue: glycoprotein; blood coagulation cascade;
XX fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;
KW proteolytic cleavage.
XX
OS Homo sapiens.
OS Synthetic.
XX
FH Key 1..19 location/Qualifiers
FT Peptide /note= "signal peptide"
FT Protein 20..2352 /note= "mature Factor VIII:C"
FT Region 20..1668 /note= "heavy chain fragment"
FT Modified-site 238 /label= "Phe, Glu, Pro"
FT /note= "inserted residue"
FT Region 1669..2351 /note= "light chain fragment"
FT Domain 751..1668 /note= "B domain"
FT
FN W09703195-A1.
PD 30-JAN-1997.
XX
XX 09-JUL-1996; 96MO-US11444.
XX
XX 11-JUL-1995; 95US-0001025.
XX
PA (CHIR ) CHIRON CORP.
XX
PI Cohen FE, Hung DT, Innis M;
DR WPI: 1997-119050/11.
XX
PT Factor VIII:C analog modified adjacent to a non-activating Arg
PT residue - used in the treatment of haemophilias, by improvement of
PT haemostasis
XX
PS Claim 8; Page -: 90pp; English.
XX
AAW11330-W11472 represent active Factor VIII:C analogues of the
CC invention. These sequences were created by mutating the wild type Factor
CC VIII:C coding sequence (see AWT51357) using mutagenic primers. The
CC analogues comprise a native Factor VIII:C polypeptide modified at a site
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC dipeptide is created. Factor VIII:C is a large glycoprotein that
CC participates in the blood coagulation cascade that ultimately converts
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC activated by plasma proteases, such as thrombin. During activation the
CC mature polypeptide is cleaved to generate heavy and light chain fragments
CC that are further cleaved. Complexes of two or more of the analogues,
CC nucleic acids and vectors encoding them may be used alone or in
CC conjunction with each other, for the prevention or treatment of active
CC Factor VIII:C deficiency in a mammal. The analogues may be used as

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immunogens to raise antibodies, and in the treatment of haemophiliacs, by improvement of haemostasis. The analogues are resistant to proteolytic cleavage and display increased plasma half-life. They may be administered at lower dosages and by different modes of administration.

Sequence 2352 AA:

Query Match 99.9%; Score 12407.5; DB 18; Length 2352.

Best Local Similarity 100.0%; Pred. No. 0;

Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

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DB 1 MOELSTCFCLLRFCFSATRRYVIGANVLSMDVMSDGLGVAPARPPRPKSPFPN 60
QY 61 TSVVYKKTLLFVEFTDHLFNIAKPRPMGLGPTIOAEVDTVVITLKMAASHPVSLAV 120
DB 61 TSVVYKKTLLFVEFTDHLFNIAKPRPMGLGPTIOAEVDTVVITLKMAASHPVSLAV 120
QY 121 GVSVMKASEGAEYDDOTSOKEKEDDVFPFGSHTVVMQVLKENGPMASDPLCLTYSLSH 180
DB 121 GVSVMKASEGAEYDDOTSOKEKEDDVFPFGSHTVVMQVLKENGPMASDPLCLTYSLSH 180
QY 121 GVSVMKASEGAEYDDOTSOKEKEDDVFPFGSHTVVMQVLKENGPMASDPLCLTYSLSH 180
DB 121 GVSVMKASEGAEYDDOTSOKEKEDDVFPFGSHTVVMQVLKENGPMASDPLCLTYSLSH 180
QY 181 VDLVNDLNSGLIGALLVCREGSLAKERTQTLHKFTLLFAVDEGKSWHSETKNSLMQ-DR 239
DB 181 VDLVNDLNSGLIGALLVCREGSLAKERTQTLHKFTLLFAVDEGKSWHSETKNSLMQ-DR 240
QY 240 DAASARAMPKMHVNGVYNSRLPGLICHRKSVYMHVIGMGTPEVHSIFLEGHFTLVN 299
DB 241 DAASARAMPKMHVNGVYNSRLPGLICHRKSVYMHVIGMGTPEVHSIFLEGHFTLVN 300
QY 300 HRQASLETSPTTELTQTLLMDLGQFLFLCHSSHQDHGMAYKVYVSCPEEQLMKNN 359
DB 301 HRQASLETSPTTELTQTLLMDLGQFLFLCHSSHQDHGMAYKVYVSCPEEQLMKNN 360
QY 360 EEAEYDDDLTDSEMDVYRFDDNSPSFQIORSVAKKPKTWVHYIAAEEEDMDYAPLV 419
DB 361 EEAEYDDDLTDSEMDVYRFDDNSPSFQIORSVAKKPKTWVHYIAAEEEDMDYAPLV 420
QY 420 APDDRSTKSYQIYLNQSPORIGKRYKRYEMAYNDEFKTRREALIOHESGILPILYXGVGDT 479
DB 421 APDDRSTKSYQIYLNQSPORIGKRYKRYEMAYNDEFKTRREALIOHESGILPILYXGVGDT 480
QY 480 LLIIIFKNQASREYNIYPHGITDVNPLYSRRLPKGVKHLKDFPILPGETFKYKMTVVEDG 539
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DB 541 PTKSDPRCLTRYSSFVNMERDLASGLIGPLICYESVDQGNQIMSDKRNVTLSVTD 600
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DB 601 ENRSWYLTENIORLLPNPAGVQLEDPFQASNTMHSINGYVDSIQLSVCLHEVAYWYL 660
QY 660 SIGAOTDFLVSFSGYTFKHKMYEDTLTLPFSGETVSMENFGMLILGCHSDPRNN 719
DB 661 SIGAOTDFLVSFSGYTFKHKMYEDTLTLPFSGETVSMENFGMLILGCHSDPRNN 720
QY 720 GMTALLKVSCKNTGDIYEDSYEDISAYLLSKNNAIEPRFSQNSRHPSTROKQFAMTT 779
DB 721 GMTALLKVSCKNTGDIYEDSYEDISAYLLSKNNAIEPRFSQNSRHPSTROKQFAMTT 780
QY 780 IPENDIEKTDPMFAHRTPMPIQONVSSDILMLRQSPPHGLSLSDLOEKAYTFESDDP 839
DB 781 IPENDIEKTDPMFAHRTPMPIQONVSSDILMLRQSPPHGLSLSDLOEKAYTFESDDP 840
QY 840 SPGALDSNNSLSDEMTHFRPOLHHSQDWFTPESGDOLRI NEKLGTATTELKIDFVSS 899
DB 841 SPGALDSNNSLSDEMTHFRPOLHHSQDWFTPESGDOLRI NEKLGTATTELKIDFVSS 900
QY 900 TSNNLISTIPSDNLAAGDNTSSLGPPSMVYHDSOLDTTLTGKAKSSPLTESGGPLSLSE 959
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DB 901 TSNNLISTIPSDNLAAGDNTSSLGPPSMVYHDSOLDTTLTGKAKSSPLTESGGPLSLSE 960
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DB 961 ENDSKILESGLMNSQESWGNKSVSTESGRLEFKGRAGPALITKDNALFKVYSISLKT 1020
QY 1020 NKTSSNNSATNRKTHIDGSPILLIENSPVNMNILESTDEFKKYVTLPHDRMLMKNATLAR 1079
DB 1021 NKTSSNNSATNRKTHIDGSPILLIENSPVNMNILESTDEFKKYVTLPHDRMLMKNATLAR 1080
QY 1080 LNHMSKTTSSKNMMEVQAKKEGPIPPDAONPDMSEFFKMLFLPESARMIQRTGKNSLNS 1139
DB 1081 LNHMSKTTSSKNMMEVQAKKEGPIPPDAONPDMSEFFKMLFLPESARMIQRTGKNSLNS 1140
QY 1140 GCGSPKOLVSLGPEKSYEGONFLISEKKNVYVKGFTKDVGLKEMVPPSSRNFLTND 1199
DB 1141 GCGSPKOLVSLGPEKSYEGONFLISEKKNVYVKGFTKDVGLKEMVPPSSRNFLTND 1200
QY 1200 NLHENNTHNOEKKIOEIEKKETLLOENVVLPQIHVTGTKNFMKNLFLSTRONVGSY 1259
DB 1201 NLHENNTHNOEKKIOEIEKKETLLOENVVLPQIHVTGTKNFMKNLFLSTRONVGSY 1260
QY 1260 DGAAPVLOPFRSLNDSTNRKTKHAHFSKKGEENLEGLGNOTQOIVEKYACTRISPN 1319
DB 1261 DGAAPVLOPFRSLNDSTNRKTKHAHFSKKGEENLEGLGNOTQOIVEKYACTRISPN 1320
QY 1320 TSQONFVTOQRKALKQFRLPLEETELEKRIYDDDTSQMSKMKHLPSLTQIDYNEK 1379
DB 1321 TSQONFVTOQRKALKQFRLPLEETELEKRIYDDDTSQMSKMKHLPSLTQIDYNEK 1380
QY 1380 EKGATQSPISDCLTRSHSIPQANRSPPLIAKVSFSPSIRPIYLRVLEFQDNSSHLPAAS 1439
DB 1381 EKGATQSPISDCLTRSHSIPQANRSPPLIAKVSFSPSIRPIYLRVLEFQDNSSHLPAAS 1440
QY 1440 YRKXDSGVQSSHFLOGAKNNLSIALITLTEMGDQREYSGISGTSATSVYKYKVENTVL 1499
DB 1441 YRKXDSGVQSSHFLOGAKNNLSIALITLTEMGDQREYSGISGTSATSVYKYKVENTVL 1500
QY 1500 PKPDLPTSGKVELLPKVHLYOKDLFPTETSNSSPGHLDVEGSLLOGEGAIKMEANR 1559
DB 1501 PKPDLPTSGKVELLPKVHLYOKDLFPTETSNSSPGHLDVEGSLLOGEGAIKMEANR 1560
QY 1560 PGKVPFLRVMTESASATPSKLDLPLAMNHNHGTQIPKEEMKSOEKSPEKTAFFKKDTLS 1619
DB 1561 PGKVPFLRVMTESASATPSKLDLPLAMNHNHGTQIPKEEMKSOEKSPEKTAFFKKDTLS 1620
QY 1620 LNAESNHAIAINEGQNKPEIEVTWAKQRTERLCSQNPVLKRHOEITRTYLOSDOE 1679
DB 1621 LNAESNHAIAINEGQNKPEIEVTWAKQRTERLCSQNPVLKRHOEITRTYLOSDOE 1680
QY 1680 ETDVDDPTISYEMKKEDPDYDDEDNOSPRSFQKTRHAFIAAVERLMDYGMSSPHYLRN 1739
DB 1681 ETDVDDPTISYEMKKEDPDYDDEDNOSPRSFQKTRHAFIAAVERLMDYGMSSPHYLRN 1740
QY 1740 RAQSGSVQFKKVVPOBFTDGSFTQPLRYGELNHLGLGTPYRAVEENIMWTRRNQAS 1799
DB 1741 RAQSGSVQFKKVVPOBFTDGSFTQPLRYGELNHLGLGTPYRAVEENIMWTRRNQAS 1800
QY 1800 RYSFYSLSIYEEDQROGAEPKRNFEVAPNETKTYFMKVYOHMAAPTKEFDCKAMAYFSD 1859
DB 1801 RYSFYSLSIYEEDQROGAEPKRNFEVAPNETKTYFMKVYOHMAAPTKEFDCKAMAYFSD 1860
QY 1860 VDLEKDVHSLIGPLVCHRTNLTINAHGRQYTVQDBALFPTITDEFKSYFVENNERCR 1919
DB 1861 VDLEKDVHSLIGPLVCHRTNLTINAHGRQYTVQDBALFPTITDEFKSYFVENNERCR 1920
QY 1920 APCNTOMEDPTFKENYFHAINGIYIMDTLPGLVYADODRIRWYLLSMGSNENIHSIHSG 1979
DB 1921 APCNTOMEDPTFKENYFHAINGIYIMDTLPGLVYADODRIRWYLLSMGSNENIHSIHSG 1980
QY 1980 HVTYVRKKEEYKALYLYLVGYEYVEMLPKSAAGIYWEVCLIEBHIAAMSTLFLYVYNSK 2039
DB 1981 HVTYVRKKEEYKALYLYLVGYEYVEMLPKSAAGIYWEVCLIEBHIAAMSTLFLYVYNSK 2040
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QY 2040 COTPLGASGHITDFOITASGOYGOMADKLARLHYSGSINAMSTKEPESWIKVDLLAPMI 2099  
DB 2041 COTPLGASGHITDFOITASGOYGOMADKLARLHYSGSINAMSTKEPESWIKVDLLAPMI 2100  
QY 2100 IHGKTGAGARQKFSLSYISQFIMYSLDGKMWQYRGNSTGTLMEYFPGNVSSGIRKINIF 2159  
DB 2101 IHGKTGAGARQKFSLSYISQFIMYSLDGKMWQYRGNSTGTLMEYFPGNVSSGIRKINIF 2160  
QY 2160 NPPIIARIYRLHPHYSIRSTLRMLMCCDINSQSMPLGMSKASISDQITASSFTNNMF 2219  
DB 2161 NPPIIARIYRLHPHYSIRSTLRMLMCCDINSQSMPLGMSKASISDQITASSFTNNMF 2220  
QY 2220 ATWSPSKARLHLQGRSNANRPVNNPKEMLOVDFOKTMKYGVYTGQVKSLLTSMYKEF 2279  
DB 2221 ATWSPSKARLHLQGRSNANRPVNNPKEMLOVDFOKTMKYGVYTGQVKSLLTSMYKEF 2280  
QY 2280 LISSSODGHOWTLFONGKVKYFGQGNDSFTPVVNSIDPPLRLRYLRILHPOSVWQIALR 2339  
DB 2281 LISSSODGHOWTLFONGKVKYFGQGNDSFTPVVNSIDPPLRLRYLRILHPOSVWQIALR 2340  
QY 2340 MEVLGCEADOLY 2351  
DB 2341 MEVLGCEADOLY 2352

RESULT 71  
AAW11333  
ID AAW11333 standard; Protein; 2352 AA.  
XX AAW11333;  
XX 17-NOV-1997 (first entry)  
DE Active Factor VIII:C analogue residue 219 P insertion.  
XX  
KM Factor VIII:C analogue; glycoprotein; blood coagulation cascade;  
KM fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KM plasma protease; thrombin; immunogen; antibody; haemophiliae; therapy;  
KM proteolytic cleavage.  
XX Homo sapiens.  
OS Synthetic.  
XX  
FH Key Location/Qualifiers  
FT Peptide 1..19  
FT /note= "signal peptide"  
FT Protein 20..2352  
FT Region /note= "mature Factor VIII:C"  
FT 20..1668  
FT /note= "heavy chain fragment"  
FT Misc-difference 239  
FT /note= "inserted residue"  
FT Region 1669..2351  
FT /note= "light chain fragment"  
FT Domain 761..1668  
FT /note= "B domain"  
XX MO9703195-A1.  
XX 30-JAN-1997.  
XX PD 09-JUL-1996; 96MO-US11444.  
XX PE 11-JUL-1995; 95US-0001025.  
XX PR (CHIR ) CHIRON CORP.  
XX Cohen FE, Hung DT, Innis M;  
XX WPI; 1997-119050/11.  
XX Factor VIII:C analog modified adjacent to a non-activating Arg

PT residue - used in the treatment of haemophiliacs, by improvement of  
PT haemostasis  
XX  
PS Claim 7; Page -: 90pp; English.  
XX  
AAW11330-W1472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC x-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophiliacs, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX  
SQ Sequence 2352 AA:  
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;  
QY 1 MQTELSTCFPLCLRLRCFSATPRRYLGAVELSDNDYMQSLGELPVDARFPRPKSPPN 60  
DB 1 MQTELSTCFPLCLRLRCFSATPRRYLGAVELSDNDYMQSLGELPVDARFPRPKSPPN 60  
QY 61 TSVYVKKTLVEFTDLNFKAKRPPRMGGLGPTQAEYDQVYVTLTKNASHPSVLAHV 120  
DB 61 TSVYVKKTLVEFTDLNFKAKRPPRMGGLGPTQAEYDQVYVTLTKNASHPSVLAHV 120  
QY 121 GVSYWKASGEAEYDDQTSQREKEDKVPFGSGHTYVYQVLKENGPMASDPLCLTYSLSH 180  
DB 121 GVSYWKASGEAEYDDQTSQREKEDKVPFGSGHTYVYQVLKENGPMASDPLCLTYSLSH 180  
QY 181 VDLVKDNLNGLIGALLVCREGSLAKERTQTLAKRFTLLFVDFEGSKMSHSEKSLMOD-R 239  
DB 181 VDLVKDNLNGLIGALLVCREGSLAKERTQTLAKRFTLLFVDFEGSKMSHSEKSLMODR 240  
QY 240 DAASARAMPKMTNVNRYVRSPLGLGCHRSYVYVYVIGMGTTPRVSILPELGHTELVNR 299  
DB 241 DAASARAMPKMTNVNRYVRSPLGLGCHRSYVYVYVIGMGTTPRVSILPELGHTELVNR 300  
QY 300 HROASLEISPTFTFQTLMDLGOFLLFCHISSHODMEAYVAVKDSCEPEQLRMKN 359  
DB 301 HROASLEISPTFTFQTLMDLGOFLLFCHISSHODMEAYVAVKDSCEPEQLRMKN 360  
QY 360 BEAEDYDDDLTDEMDVYVRFDDNSPFIQIRSAKAKHKPTVWVYIAAEEEDMVAPLYL 419  
DB 361 BEAEDYDDDLTDEMDVYVRFDDNSPFIQIRSAKAKHKPTVWVYIAAEEEDMVAPLYL 420  
QY 420 APDDRYSQYLNNNGFORIGRKYKVRPMYVTEBTKREALQHSGLTGLYGEVGT 479  
DB 421 APDDRYSQYLNNNGFORIGRKYKVRPMYVTEBTKREALQHSGLTGLYGEVGT 480  
QY 480 LLIIFKQASRPYNYIPGIDTVRPLYSRLPGVKHLKDFPLPGLFETKKTWTVYEDG 539  
DB 481 LLIIFKQASRPYNYIPGIDTVRPLYSRLPGVKHLKDFPLPGLFETKKTWTVYEDG 540  
QY 540 PTKSDPRLCTRRYYSFVNNERDLASGLTGLPYKESYDQGNQIMSDKRNVTLSVED 599  
DB 541 PTKSDPRLCTRRYYSFVNNERDLASGLTGLPYKESYDQGNQIMSDKRNVTLSVED 600  
QY 600 EBRSMVLTENIQRLFPNPGVQLDEDPERQSNIMHSINQYVDSQLSLVCHEAVAYWYL 659

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Db      601 ENRSMYLTENIQRFLEPNAGVOLDEPFOASNIMHSINGYVDSIQLSVCIHEVAWYIL 660
Qy      660 SIGAQDTFLSPFSGVTEFKHKMYEDLTLTLPFSGETVMSNENGLMILGCHNSFRNR 719
Db      661 SIGAQDTFLSPFSGVTEFKHKMYEDLTLTLPFSGETVMSNENGLMILGCHNSFRNR 720
Qy      720 GMTALLKVSCKNKGDDYEDSYEDISAYLLSKNNAIEPRSPQNSRHPSTROKOFNATT 779
Db      721 GMTALLKVSCKNKGDDYEDSYEDISAYLLSKNNAIEPRSPQNSRHPSTROKOFNATT 780
Qy      780 IPEMDIEKTDPMFAHRTMPKIQNVSSDDLMLLRSPTHGLSLSDIQEAKYTEFSDDP 839
Db      781 IPEMDIEKTDPMFAHRTMPKIQNVSSDDLMLLRSPTHGLSLSDIQEAKYTEFSDDP 840
Qy      840 SPGAIDSNNSLSMTHFRPOLHSGDWYFTPEGSLQRLNEKLTGTTATELTKIDPFVSS 899
Db      841 SPGAIDSNNSLSMTHFRPOLHSGDWYFTPEGSLQRLNEKLTGTTATELTKIDPFVSS 900
Qy      900 TSNNLISTPSDNMLAAGTDNTSSLGPPSMVHYHDSQDITTLFGKSSPLTSGGPTLSLSE 959
Db      901 TSNNLISTPSDNMLAAGTDNTSSLGPPSMVHYHDSQDITTLFGKSSPLTSGGPTLSLSE 960
Qy      960 ENDSKILLESGLMANSOESSMGKNVSTESGRLFKGRAGPALTLKDNALFEKYSISILKT 1019
Db      961 ENDSKILLESGLMANSOESSMGKNVSTESGRLFKGRAGPALTLKDNALFEKYSISILKT 1020
Qy      1020 NKTSSNATNRKTHIDGSPSLIENSPSWONILIESDTEFKKTYPLIHDMIMDKNATLAR 1079
Db      1021 NKTSSNATNRKTHIDGSPSLIENSPSWONILIESDTEFKKTYPLIHDMIMDKNATLAR 1080
Qy      1080 LNHMSNKTSSKMEWVQKKGGPIPPDAQNPDMSEFKMLFPEBARHIOQTHKNSLNS 1139
Db      1081 LNHMSNKTSSKMEWVQKKGGPIPPDAQNPDMSEFKMLFPEBARHIOQTHKNSLNS 1140
Qy      1140 GGGSPKQVLSIGPEKSVBGNFLSEKKNVYVNGEFTDVGLKEMVPPSSRNLFITND 1199
Db      1141 GGGSPKQVLSIGPEKSVBGNFLSEKKNVYVNGEFTDVGLKEMVPPSSRNLFITND 1200
Qy      1200 NLHENHNOEKKIOEIEKKTLLIOENVVLPOLHVTGKKNMKNLPLSTRONVGSY 1259
Db      1201 NLHENHNOEKKIOEIEKKTLLIOENVVLPOLHVTGKKNMKNLPLSTRONVGSY 1260
Qy      1260 DGATAPVLODFRSLNSTRKTKTAHRSKGBEENLEGLQOTQIYEKACTRISPN 1319
Db      1261 DGATAPVLODFRSLNSTRKTKTAHRSKGBEENLEGLQOTQIYEKACTRISPN 1320
Qy      1320 TSQONFVTOQRKALQOFLPLEETELBKRIIVDDSTQMSKNMKHLPTSTLQIDYNEK 1379
Db      1321 TSQONFVTOQRKALQOFLPLEETELBKRIIVDDSTQMSKNMKHLPTSTLQIDYNEK 1380
Qy      1380 EKGAITOSPLSDCLTRSHSIPQANSRPLPIKVSFSPSTIRPIYLRVLFQONSSHLPAS 1439
Db      1381 EKGAITOSPLSDCLTRSHSIPQANSRPLPIKVSFSPSTIRPIYLRVLFQONSSHLPAS 1440
Qy      1440 YRKDGVOSSSHFLOGAKNNLSLAILTLEMTGDQEHVSGTSAITSYTKKVENTVL 1499
Db      1441 YRKDGVOSSSHFLOGAKNNLSLAILTLEMTGDQEHVSGTSAITSYTKKVENTVL 1500
Qy      1500 PKPDLPTSGVELLPRVHIYOKDLFPEYENSGSPGHLIDVEGSLQTEGAIKWNBANR 1559
Db      1501 PKPDLPTSGVELLPRVHIYOKDLFPEYENSGSPGHLIDVEGSLQTEGAIKWNBANR 1560
Qy      1560 PGKVPFLRVATESSATPKLIDPLAMNHNHGTQIPEEKKSQESPEKTAFFKKDDITLS 1619
Db      1561 PGKVPFLRVATESSATPKLIDPLAMNHNHGTQIPEEKKSQESPEKTAFFKKDDITLS 1620
Qy      1620 LMACESNHAIJAINEGONKPEIEVTWAKOGTEBFLCSQNPVYAKRHOREITRTLLSQDE 1679
Db      1621 LMACESNHAIJAINEGONKPEIEVTWAKOGTEBFLCSQNPVYAKRHOREITRTLLSQDE 1680
Qy      1680 EIDYDDTISVEMKKEFDIYDEDENOSPRQKTRHFIATAERLMDYGMSSPHVLRN 1739

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Db      1681 EIDYDDTISVEMKKEFDIYDEDENOSPRQKTRHFIATAERLMDYGMSSPHVLRN 1740
Qy      1740 RAQSGVPOFKKRVYFOEFTDGSFTQPLRYGELNEHLGLGPYIAEVEDNIMYTFRNOAS 1799
Db      1741 RAQSGVPOFKKRVYFOEFTDGSFTQPLRYGELNEHLGLGPYIAEVEDNIMYTFRNOAS 1800
Qy      1800 RPYFSYSLISYEEDQROGAEPRKNEFKPRNETKYTFWKVOHMAPTKDEFDCKAMAFSD 1859
Db      1801 RPYFSYSLISYEEDQROGAEPRKNEFKPRNETKYTFWKVOHMAPTKDEFDCKAMAFSD 1860
Qy      1860 VDLEKDYHSLGLPRLVCHNTWTLNPAARGOYVQOEALFPTIPDETSMYTFEMERNCR 1919
Db      1861 VDLEKDYHSLGLPRLVCHNTWTLNPAARGOYVQOEALFPTIPDETSMYTFEMERNCR 1920
Qy      1920 APCNIQWEDPTEKERNRHAINGYIMDTLPLGLVMAODRIRWYLLISMGSENIHSHIESG 1979
Db      1921 APCNIQWEDPTEKERNRHAINGYIMDTLPLGLVMAODRIRWYLLISMGSENIHSHIESG 1980
Qy      1980 HFTVVRKKEEYKMAALNYLPGVFETVEMLPKAGIWRVBCLGELHAGNSTLFLVYSNK 2039
Db      1981 HFTVVRKKEEYKMAALNYLPGVFETVEMLPKAGIWRVBCLGELHAGNSTLFLVYSNK 2040
Qy      2040 CQTEPLMASGHIRDOITASQOYQMAPKLARLHSGSINASTKEPPSMYKVDLAPMI 2099
Db      2041 CQTEPLMASGHIRDOITASQOYQMAPKLARLHSGSINASTKEPPSMYKVDLAPMI 2100
Qy      2100 IHGIKTQAGOKESSLYISOFLIMYSIDGKKMOTYRGNSGTGLMVFQNDSSGIRKHNIF 2159
Db      2101 IHGIKTQAGOKESSLYISOFLIMYSIDGKKMOTYRGNSGTGLMVFQNDSSGIRKHNIF 2160
Qy      2160 NPPIIARYIRLHPHTYSIRSTLRBELMGCOLNCSMPGLMESKAIASDAQIATASYTFNMF 2219
Db      2161 NPPIIARYIRLHPHTYSIRSTLRBELMGCOLNCSMPGLMESKAIASDAQIATASYTFNMF 2220
Qy      2220 ATWSPSKARLHLQGSNMAKROVNNPKEMIQVFOCTAKVYVYTTQCYKSLISMVYKFE 2279
Db      2221 ATWSPSKARLHLQGSNMAKROVNNPKEMIQVFOCTAKVYVYTTQCYKSLISMVYKFE 2280
Qy      2280 LISSQDQHOWTLTFPONGKVKVFGONDSEFTPVVNSLDPLLTRYLRIHQSWVHOIALR 2339
Db      2281 LISSQDQHOWTLTFPONGKVKVFGONDSEFTPVVNSLDPLLTRYLRIHQSWVHOIALR 2340
Qy      2340 MEVLGCEADQDLY 2351
Db      2341 MEVLGCEADQDLY 2352

RESULT 72
AAW11334
ID AAW11334 standard; Protein: 2352 AA.
XX
AC AAW11334;
XX
DT 17-NOV-1997 (first entry)
XX
DE Active Factor VIII:C analogue residue 220 P Insertion.
XX
KW Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;
XX
OS Homo sapiens.
OS Synthetic.
XX
FH Key 1..19 Location/Qualifiers
FT Peptide /note= "signal peptide"
FT Protein 20..2352 /note= "mature Factor VIII:C"
FT Region 20..1668 /note= "heavy chain fragment"
FT Misc-difference 240

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FT	/note- "inserted residue"
FT	Region
FT	1669..2351
FT	/note- "light chain fragment"
FT	Domain
FT	761..1668
FT	/note- "B domain"
XX	
PN	MO9703195-A1.
XX	
FD	30-JAN-1997.
XX	
XX	09-JUL-1996; 96WO-US11444.
XX	
PR	11-JUL-1995; 95US-0001025.
PA	(CHIR ) CHIRON CORP.
XX	
PI	Cohen FE, Hung DT, Innis M;
XX	
DR	WPI; 1997-119050/11.
XX	
PT	Factor VIII:C analog modified adjacent to a non-activating Arg
PT	residue - used in the treatment of haemophilias, by improvement of
XX	haemostasis
XX	
PS	Claim 7; Page -: 90pp; English.
XX	
CC	AAW1330-M1472 represent active Factor VIII:C analogues of the
CC	invention. These sequences were created by mutating the wild type Factor
CC	VIII:C coding sequence (see AAF15137) using mutagenic primers. The
CC	analogues comprise a native Factor VIII:C polypeptide modified at a site
CC	adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC	dipeptide is created. Factor VIII:C is a large glycoprotein that
CC	participates in the blood coagulation cascade that ultimately converts
CC	soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC	deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC	X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC	activated by plasma proteases, such as thrombin. During activation the
CC	mature polypeptide is cleaved to generate heavy and light chain fragments
CC	that are further cleaved. Complexes of two or more of the analogues,
CC	nucleic acids and vectors encoding them may be used alone or in
CC	conjunction with each other, for the prevention or treatment of active
CC	Factor VIII:C deficiency in a mammal. The analogues may be used as
CC	immunogens to raise antibodies, and in the treatment of haemophilias, by
CC	improvement of haemostasis. The analogues are resistant to proteolytic
CC	cleavage and display increased plasma half-life. They may be administered
CC	at lower dosages and by different modes of administration.
XX	
XX	Sequence 2352 AA:
XX	
Query Match	99.9%; Score 12407.5; DB 18; Length 2352;
Best Local Similarity	100.0%; Pred. No. 0;
Matches 2351; Conservative	0; Mismatches 0; Indels 1; Gaps 1;
QY	1 MOELSTCFELCLLRFCFSATRRYYLGAVELSMQSDLGELPVDARPPRPVPSFPFN 60
DB	1 MOELSTCFELCLLRFCFSATRRYYLGAVELSMQSDLGELPVDARPPRPVPSFPFN 60
QY	61 TSVYKKTLPEFPHLFINAKRPPRMGLIGPTIOAEVVDVYTLTKMASSHPVSLHAY 120
DB	61 TSVYKKTLPEFPHLFINAKRPPRMGLIGPTIOAEVVDVYTLTKMASSHPVSLHAY 120
QY	121 GSVYKASSEGAEDDDTSQREKEDDKVPFGSSHYYVQVLEKNGPMASDPICLTLYSLH 180
DB	121 GSVYKASSEGAEDDDTSQREKEDDKVPFGSSHYYVQVLEKNGPMASDPICLTLYSLH 180
QY	181 VDLVKDNLNSGLIGALLVYCRGSLAKEKTOYLHRTLLFAVDEGSKSMHSETKNSLMODR 239
DB	181 VDLVKDNLNSGLIGALLVYCRGSLAKEKTOYLHRTLLFAVDEGSKSMHSETKNSLMODR 240
QY	240 DAASARAMPKMTHTYNGVYNSRLPGLIGCHRSYVWHYTGITTPVHASTFLDEGHTFLVNR 299
DB	241 DAASARAMPKMTHTYNGVYNSRLPGLIGCHRSYVWHYTGITTPVHASTFLDEGHTFLVNR 300
QY	300 HROAKLEISPTTFLTAQTLLMDLGGFLFCHISSHODGMEAYVYKVDSCPEPOLRMKN 359
DB	301 HROAKLEISPTTFLTAQTLLMDLGGFLFCHISSHODGMEAYVYKVDSCPEPOLRMKN 360
QY	360 EBAEDYDDDLTDSMAVYRPDDDNSSPQTORSVAKKHPTWVHYTAAEEDMDYAPVL 419
DB	361 EBAEDYDDDLTDSMAVYRPDDDNSSPQTORSVAKKHPTWVHYTAAEEDMDYAPVL 420
QY	420 APDDRYSQYLANNGPORGKRYKRYRMAYTDEFTKTBRAIOHESGLIGLXGEGVD 479
DB	421 APDDRYSQYLANNGPORGKRYKRYRMAYTDEFTKTBRAIOHESGLIGLXGEGVD 480
QY	480 LLITFKNOSRPVNTYPHGTTDPRPLYSRLPKGVKHLKOPLLPEETFKYKWTYVDG 539
DB	481 LLITFKNOSRPVNTYPHGTTDPRPLYSRLPKGVKHLKOPLLPEETFKYKWTYVDG 540
QY	540 PTKSDPRLTRYSSFYVNERDLASGLIGPLLIKCSVDQRCNOIMSDKRVLLFSYVD 599
DB	541 PTKSDPRLTRYSSFYVNERDLASGLIGPLLIKCSVDQRCNOIMSDKRVLLFSYVD 600
QY	600 ENRSWYLTENIORFLPNPAGVQLEDPFEOASIMHNSINGVFPDQLSVCLHEVAVYIL 659
DB	601 ENRSWYLTENIORFLPNPAGVQLEDPFEOASIMHNSINGVFPDQLSVCLHEVAVYIL 660
QY	660 STGAOTDFLSVFSGYTFKKMYEDTLTPPESGEYVPMENPGLMILGCHNSDPNR 719
DB	661 STGAOTDFLSVFSGYTFKKMYEDTLTPPESGEYVPMENPGLMILGCHNSDPNR 720
QY	720 GMTALLKVSQCKNTGYEDSYEDISAVLLSKNNAIEPFSQNSRHPSTROKOFNAT 779
DB	721 GMTALLKVSQCKNTGYEDSYEDISAVLLSKNNAIEPFSQNSRHPSTROKOFNAT 780
QY	780 IPENDIEETDWFHRTPMKIKIONVSSDLMALROSPPHGSLDLOEAYEFSSDP 839
DB	781 IPENDIEETDWFHRTPMKIKIONVSSDLMALROSPPHGSLDLOEAYEFSSDP 840
QY	840 SGCAIDSNNSISEMTHRPQLHNSGMYTPBSGLQRLNEKIGTTAAELKLDKFKSS 899
DB	841 SGCAIDSNNSISEMTHRPQLHNSGMYTPBSGLQRLNEKIGTTAAELKLDKFKSS 900
QY	900 TSNNLITIPSDNLAAQDWTSSIGPPSPVHYDSOLDTLTFGKSSPLTESGGLSLSE 959
DB	901 TSNNLITIPSDNLAAQDWTSSIGPPSPVHYDSOLDTLTFGKSSPLTESGGLSLSE 960
QY	960 ENNDSKLLSEGLMSQSSMGKVVSTESGRLPFGKRAHGPALLTDNMLFVYSILTK 1019
DB	961 ENNDSKLLSEGLMSQSSMGKVVSTESGRLPFGKRAHGPALLTDNMLFVYSILTK 1020
QY	1020 NKTSNNSATNKKTHIDPSLLIENSPWQNTLSDBEKKVTPLIHDMALDKNAATLR 1079
DB	1021 NKTSNNSATNKKTHIDPSLLIENSPWQNTLSDBEKKVTPLIHDMALDKNAATLR 1080
QY	1080 LNHMSNKTSSKNMENVQCKKEGPIPPDAONPDMSFFRMLFLPESARWIORHGNKSLNS 1139
DB	1081 LNHMSNKTSSKNMENVQCKKEGPIPPDAONPDMSFFRMLFLPESARWIORHGNKSLNS 1140
QY	1140 GGGSPKOLVSLGPEKVEGQNTLSKKNVYVVGEGEPKQVGLKEWAPSSRNLFETMLD 1199
DB	1141 GGGSPKOLVSLGPEKVEGQNTLSKKNVYVVGEGEPKQVGLKEWAPSSRNLFETMLD 1200
QY	1200 NLHENNTNHOEKKIOEIEKEKTLIOENVVLPOLHTYTGKFNKMKJLLSTRONVEGSY 1259
DB	1201 NLHENNTNHOEKKIOEIEKEKTLIOENVVLPOLHTYTGKFNKMKJLLSTRONVEGSY 1260
QY	1260 DGAYVAVLPDPRSLNDSNTNKTTHNHSKGEENLEGGNTOIYKVACTTRISPN 1319
DB	1261 DGAYVAVLPDPRSLNDSNTNKTTHNHSKGEENLEGGNTOIYKVACTTRISPN 1320
QY	1320 TSOQNFVTONSKRALKOPFLPEETBLEKRIIIVDTSTQSKMKMLPSTLTQIDVYEK 1379
DB	1321 TSOQNFVTONSKRALKOPFLPEETBLEKRIIIVDTSTQSKMKMLPSTLTQIDVYEK 1380
QY	1380 EKGATIOSPLSDCLTRSHSIPQANSPLPIAKVSSPSPRIYLTFRVLFDONSSHLPAS 1439

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Db      1381 EKGALTQPSLSDCLTNRSHSIPQANKRSPPLIAVNSFSPISRPITYLTRVLYQDNSSHLPAAS 1440
Qy      1440 YRRKDSGVQESSHFLQAGAKKNMNLSLAILTLEMTGDQREVSGSLGTSATNSVYTKKVENTVL 1499
Db      1441 YRRKDSGVQESSHFLQAGAKKNMNLSLAILTLEMTGDQREVSGSLGTSATNSVYTKKVENTVL 1500
Qy      1500 PKPDLPTKSGVELLPVHYHOKDLFPTETSGNSGHLIDVEGSLLOGTGALAKNNEAR 1559
Db      1501 PKPDLPTKSGVELLPVHYHOKDLFPTETSGNSGHLIDVEGSLLOGTGALAKNNEAR 1560
Qy      1560 PGKVPFLRVATSSAKTPSKLLDPLAMDNHYGTQIPKEEMKSOEKSPKTAFFKKKTITIS 1619
Db      1561 PGKVPFLRVATSSAKTPSKLLDPLAMDNHYGTQIPKEEMKSOEKSPKTAFFKKKTITIS 1620
Qy      1620 LNACSNHAIANINGCONKPEIEVTANAKGRTERLCSQNPVLRHQREITRTTLOSDQE 1679
Db      1621 LNACSNHAIANINGCONKPEIEVTANAKGRTERLCSQNPVLRHQREITRTTLOSDQE 1680
Qy      1680 EIDYDDTISVEKKEDPDYIDEDENSPSPFOKTRHFIAAVERLMDYGMSSPHVLRN 1739
Db      1681 EIDYDDTISVEKKEDPDYIDEDENSPSPFOKTRHFIAAVERLMDYGMSSPHVLRN 1740
Qy      1740 RAQSGSVPOFKKVFQEFQDTSFTQPLYRGELNEHLGLGPYIRAEVEDNIMVTFRNQAS 1799
Db      1741 RAQSGSVPOFKKVFQEFQDTSFTQPLYRGELNEHLGLGPYIRAEVEDNIMVTFRNQAS 1800
Qy      1800 RPYSTFSSLISEEDQROGAPRKNFYKPNERTYPMKQOHMAPTQDEPCKAMAYFSD 1859
Db      1801 RPYSTFSSLISEEDQROGAPRKNFYKPNERTYPMKQOHMAPTQDEPCKAMAYFSD 1860
Qy      1860 VDLEKDVHSGLIGPLVCHTNTLPAHAGROYVQEFALFTLFEDETKSWYFTEEMERNC 1919
Db      1861 VDLEKDVHSGLIGPLVCHTNTLPAHAGROYVQEFALFTLFEDETKSWYFTEEMERNC 1920
Qy      1920 APCNIQMEDPTFKENYRRHAINGYIMDPLGIMADODIRMYLLSMGNSNHSIHFSG 1979
Db      1921 APCNIQMEDPTFKENYRRHAINGYIMDPLGIMADODIRMYLLSMGNSNHSIHFSG 1980
Qy      1980 HVEFTVRKKEEYKMAIYNLYPGVFETVEMLPKAGIWRVECLLGEHLHAGNSTLFLVYSNK 2039
Db      1981 HVEFTVRKKEEYKMAIYNLYPGVFETVEMLPKAGIWRVECLLGEHLHAGNSTLFLVYSNK 2040
Qy      2040 CQPLGASGHIRDRQITASGOYGOMAPKLARLHYSGSINAMSTPEPSMIKVDLAPMI 2099
Db      2041 CQPLGASGHIRDRQITASGOYGOMAPKLARLHYSGSINAMSTPEPSMIKVDLAPMI 2100
Qy      2100 IHGKTQGARQKFFSLYISQFTIMYSLDGKKWQTYRGNSTGILAMPFGNDVSSGKHNIF 2159
Db      2101 IHGKTQGARQKFFSLYISQFTIMYSLDGKKWQTYRGNSTGILAMPFGNDVSSGKHNIF 2160
Qy      2160 NPPIIARYIRLHPTHYSIRSLRMELMCDLNSCAMPKESKASISDAQITASSYFTNMF 2219
Db      2161 NPPIIARYIRLHPTHYSIRSLRMELMCDLNSCAMPKESKASISDAQITASSYFTNMF 2220
Qy      2220 ATWSPSKARHLQGRNARNRPVNNPKEMLOVDQKMKATGYTTQGVASLITSMYKEF 2279
Db      2221 ATWSPSKARHLQGRNARNRPVNNPKEMLOVDQKMKATGYTTQGVASLITSMYKEF 2280
Qy      2280 LISSSDGHQMTLFPQNGKVKVFGQNDSTFPVNSLDPPLRLRYLRHIPSQWQIALR 2339
Db      2281 LISSSDGHQMTLFPQNGKVKVFGQNDSTFPVNSLDPPLRLRYLRHIPSQWQIALR 2340
Qy      2340 MEVLGCEAODLY 2351
Db      2341 MEVLGCEAODLY 2352

```

## RESULT 73

AAW11336

ID AAW11336 standard; Protein; 2352 AA.

XX AAW11336;

```

XX      17-NOV-1997 (first entry)
DT      Active Factor VIII:C analogue residue 225 P insertion.
XX      DE
XX      KW Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW      fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
XX      plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
XX      proteolytic cleavage.
OS      Homo sapiens.
XX      OS
XX      FH Synthetic.
XX      FH Key
XX      FH Location/Qualifiers
FH      Peptide
FH      /note="signal peptide"
FH      Protein
FH      /note="20..2352"
FH      Region
FH      /note="mature Factor VIII:C"
FH      /note="20..1668"
FH      /note="heavy chain fragment"
FH      /note="245"
FH      /note="inserted residue"
FH      Region
FH      /note="1669..2351"
FH      /note="light chain fragment"
FH      /note="761..1668"
FH      Domain
FH      /note="B domain"
XX      W09703195-A1.
XX      PD 30-JAN-1997.
XX      PF 09-JUL-1996; 96W0-0511444.
XX      PR 11-JUL-1995; 95U5-0001025.
XX      PA (CHIR ) CHIRON CORP.
XX      DR Cohen FE, Hung DT, Innis M;
XX      WPI; 1997-119050/11.
XX      CC Factor VIII:C analog modified adjacent to a non-activating Arg
XX      residue - used in the treatment of haemophiliacs, by improvement of
XX      PT haemostasis
XX      PS Claim 9; Page -: 90pp; English.
XX      AA
XX      AAW11330-W11472 represent active Factor VIII:C analogues of the
XX      invention. These sequences were created by mutating the wild type Factor
XX      VIII:C coding sequence (see AAF51357) using mutagenic primers. The
XX      analogues comprise a native Factor VIII:C polypeptide modified at a site
XX      adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
XX      dipeptide is created. Factor VIII:C is a large glycoprotein that
XX      participates in the blood coagulation cascade that ultimately converts
XX      soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
XX      deficiency in Factor VIII:C is responsible for haemophilia A, which is an
XX      X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
XX      matured by plasma proteases, such as thrombin. During activation the
XX      mature polypeptide is cleaved to generate heavy and light chain fragments
XX      that are further cleaved. Complexes of two or more of the analogues,
XX      nucleic acids and vectors encoding them may be used alone or in
XX      conjunction with each other, for the prevention or treatment of active
XX      Factor VIII:C deficiency in a mammal. The analogues may be used as
XX      immunogens to raise antibodies, and in the treatment of haemophiliacs, by
XX      cleavage and display increased plasma half-life. They may be administered
XX      at lower dosages and by different modes of administration.
XX      SQ Sequence 2352 AA;
XX
XX      Query Match 99.9%; Score 12407.5; DB 18; Length 2352;
XX      Best Local Similarity 100.0%; Pred. No. 0;
XX      Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

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QY 1 MOELSTCFPLCLLRCSATRRYVAGAVELSMYDQOSDLGELPDVAFRRPRVKSPPFN 60  
1 MOELSTCFPLCLLRCSATRRYVAGAVELSMYDQOSDLGELPDVAFRRPRVKSPPFN 60  
Db 1 MOELSTCFPLCLLRCSATRRYVAGAVELSMYDQOSDLGELPDVAFRRPRVKSPPFN 60  
QY 61 TSYYKKTLEVEFTDHLFNIAKPRPMWGLGPTIOAEYDVTVTTLKNMASHVSLHAV 120  
61 TSYYKKTLEVEFTDHLFNIAKPRPMWGLGPTIOAEYDVTVTTLKNMASHVSLHAV 120  
Db 61 TSYYKKTLEVEFTDHLFNIAKPRPMWGLGPTIOAEYDVTVTTLKNMASHVSLHAV 120  
QY 121 GVSYWKASGEAEYDQTSQREKEDKVPFGSGSHYVWQVLKENGPMASDPLCTLYSYLSH 180  
121 GVSYWKASGEAEYDQTSQREKEDKVPFGSGSHYVWQVLKENGPMASDPLCTLYSYLSH 180  
Db 121 GVSYWKASGEAEYDQTSQREKEDKVPFGSGSHYVWQVLKENGPMASDPLCTLYSYLSH 180  
QY 181 VDLVKDNLNSGLIGALLVCBESLAKETQTLHKFTLLFAVFBGKSMHSTKNSLMDRD 240  
181 VDLVKDNLNSGLIGALLVCBESLAKETQTLHKFTLLFAVFBGKSMHSTKNSLMDRD 240  
Db 181 VDLVKDNLNSGLIGALLVCBESLAKETQTLHKFTLLFAVFBGKSMHSTKNSLMDRD 240  
QY 241 AASA - RAMPKMTVNGYVNRSLPGLIGCHRSYVMHVIQMTTPEVHSIFLEGHTLVNR 299  
241 AASA - RAMPKMTVNGYVNRSLPGLIGCHRSYVMHVIQMTTPEVHSIFLEGHTLVNR 299  
Db 241 AASA - RAMPKMTVNGYVNRSLPGLIGCHRSYVMHVIQMTTPEVHSIFLEGHTLVNR 299  
QY 300 HROASLEISPTFLTAQTLMDLGOFLFCHISSHQDGEAYVAVDSCPEEPOLRRKN 359  
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Db 421 APDRSYKSOYLNNNGFORIGRKYKRVPRMAYTDETFREAIQHSGLIGLGEVDT 480  
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480 LLIIFKKNQARPNYNIPIHGTDPVRLYSRRLPGVYHILKDFPLIGELIFKMTVYEDG 539  
Db 481 LLIIFKKNQARPNYNIPIHGTDPVRLYSRRLPGVYHILKDFPLIGELIFKMTVYEDG 540  
QY 540 PTKSDPRCLTRYSSSVNNERDLASGLIGPLICYKESVDQRONOJMSDKRNVILFSEVD 599  
540 PTKSDPRCLTRYSSSVNNERDLASGLIGPLICYKESVDQRONOJMSDKRNVILFSEVD 599  
Db 541 PTKSDPRCLTRYSSSVNNERDLASGLIGPLICYKESVDQRONOJMSDKRNVILFSEVD 600  
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Db 661 SIGAOTDELSVFFSGYTFKHVYVEDTLTPRPSGETVFKSMENGLMILCCHNSDRNR 720  
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QY 900 TSNNLISTIPSDMLAAGTDNNTSSLPSPMPVHYDSQIDTTLFGKSSPLTESGGPLSLSE 959  
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QY 2340 MEVLGCEADPLY 2351  
Db 2341 MEVLGCEADPLY 2352  
RESULT 74  
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ID AAW11337 standard; Protein: 2352 AA.  
AC AAW11337;  
XX  
DT 17-NOV-1997 (first entry)  
DE Active Factor VIII:C analogue residue 226 P insertion.  
XX  
KM Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;  
KM fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KM plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;  
KM proteolytic cleavage.  
XX  
OS Homo sapiens.  
OS Synthetic.  
XX  
FH Key Location/Qualifiers  
FT Peptide 1..19  
FT /note= "signal peptide"  
FT Protein 20..2352  
FT /note= "mature Factor VIII:C"  
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FT /note= "heavy chain fragment"  
FT Misc-difference 246  
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FT /note= "light chain fragment"  
FT Domain 761..1668  
FT /note= "B domain"  
XX  
PN MO9703195-A1.  
PD 30-JAN-1997.  
XX  
PF 09-JUL-1996; 96MO-US11444.  
XX  
PR 11-JUL-1995; 95US-0001025.  
XX  
PA (CHIR ) CHIRON CORP.  
PI Cohen FE, Hung DT, Innis M;  
XX  
DR WPI: 1997-119050/11.  
XX  
PT Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophilias, by improvement of  
PT haemostasis  
XX  
PS Claim 9; Page -: 90pp; English.  
CC  
CC AAW11330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAW11337) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg

CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophilias, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX  
SQ Sequence 2352 AA:  
Query Match 99.9%; Score 12407.5; DB 18; Length 2352;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;  
QY 1 MOELSTCFPLCLLRCSATRRYLLGAELSDYQSDLGELPDAFPPRPKSPFN 60  
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QY 61 TSYYKKTLFEPTDHLFNIAKPRPMMGLGPTIOAEVYDVVITLKNASHPVSLHAV 120  
Db 61 TSYYKKTLFEPTDHLFNIAKPRPMMGLGPTIOAEVYDVVITLKNASHPVSLHAV 120  
QY 121 GVSYYKASBEAGYDDQTSOREKEDKKYFGSGHYWQYLKENGPMASDPLCLTYSLSH 180  
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Db 361 EADYDDDLTISEMDYVAFDDNSPSFQIRSVAKKHKTWVHIAEBEDMDYAPLV 420  
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Db 481 LLIIFKNOARPNYNYPIGIDVRLSRKLPBGVNLKDPFLLPGEFKKYKMYVNEG 539  
QY 540 PTKSDPRCLTRYYSFVNMERDLASGLIGPLLICYESVDQNGNIMSKRNVILFSVD 599  
Db 540 PTKSDPRCLTRYYSFVNMERDLASGLIGPLLICYESVDQNGNIMSKRNVILFSVD 599  
QY 600 ENRSWYITENIOFLPNPAGVOLDEPFOASNMHSINGYVDSIQSLCHVAVAYTL 659  
Db 600 ENRSWYITENIOFLPNPAGVOLDEPFOASNMHSINGYVDSIQSLCHVAVAYTL 659  
QY 661 SIGAQDFFLSVFSGYTRKHMYEDTLTPPSGTYVMSKENVGLIICNSDFRR 719  
Db 661 SIGAQDFFLSVFSGYTRKHMYEDTLTPPSGTYVMSKENVGLIICNSDFRR 719  
QY 720 GMTALLKLVSSCDKNTGDEYEDSYDISAYLLSNNAIEPRSSONSRRPSTROKQNPAT 779  
Db 720 GMTALLKLVSSCDKNTGDEYEDSYDISAYLLSNNAIEPRSSONSRRPSTROKQNPAT 779  
QY 771 GMTALLKLVSSCDKNTGDEYEDSYDISAYLLSNNAIEPRSSONSRRPSTROKQNPAT 780  
Db 771 GMTALLKLVSSCDKNTGDEYEDSYDISAYLLSNNAIEPRSSONSRRPSTROKQNPAT 780

Qy	760	1PBNDDIKTDPWFARHTPMPK1QIOWSSDL1MLLKQSPFPHGSLSDLOEAKETFPDDP	839
Dp	761	1PBNDDIKTDPWFARHTPMPK1QIOWSSDL1MLLKQSPFPHGSLSDLOEAKETFPDDP	840
Qy	840	SPGADISNNLSLSEMTHFRRPOLHSHGDDVFPFESSGLOLRINKELGTTTATETKLKLPFKVSS	899
Dp	841	SPGADISNNLSLSEMTHFRRPOLHSHGDDVFPFESSGLOLRINKELGTTTATETKLKLPFKVSS	900
Qy	900	TSNNL1STPSDMLAAGDNTSSIGSPSMVHYNDSDLOPTLTPGKSSPLTEESGSPLSISE	959
Dp	901	TSNNL1STPSDMLAAGDNTSSIGSPSMVHYNDSDLOPTLTPGKSSPLTEESGSPLSISE	960
Qy	960	ENNDSKLLESGLIMNSOESSMKNVN5TESGRLEFKGRARHALLTKDMALFKV5ISLKT	1019
Dp	961	ENNDSKLLESGLIMNSOESSMKNVN5TESGRLEFKGRARHALLTKDMALFKV5ISLKT	1020
Qy	1020	NKTSNNSATRKRIHIGPSLLIENSPPWOMN1LESPTERKVTYPLIDHRLMOKNATYLR	1079
Dp	1021	NKTSNNSATRKRIHIGPSLLIENSPPWOMN1LESPTERKVTYPLIDHRLMOKNATYLR	1080
Qy	1080	LNMHSKTTSSKMKEMVQCKKEGPPDPAONPOMSPFKMLPLPSPAM1ORTHGKSLNS	1139
Dp	1081	LNMHSKTTSSKMKEMVQCKKEGPPDPAONPOMSPFKMLPLPSPAM1ORTHGKSLNS	1140
Qy	1140	GOGSPKQVLSLIGPEKSVGONFLSEKNKVVYVKGEGFTKDGLKEMVPSSRNLFLYND	1199
Dp	1141	GOGSPKQVLSLIGPEKSVGONFLSEKNKVVYVKGEGFTKDGLKEMVPSSRNLFLYND	1200
Qy	1200	NLHEHNTNHNEK1TOEIKETL1OENVVLPP1HVTNTRKFNKNLFL1STONVEGY	1259
Dp	1201	NLHEHNTNHNEK1TOEIKETL1OENVVLPP1HVTNTRKFNKNLFL1STONVEGY	1260
Qy	1260	DGAAPRLODFRSLDNTNRTKKTARFSSKGEENLBDLGNQTKO1VERKACTTP1ISN	1319
Dp	1261	DGAAPRLODFRSLDNTNRTKKTARFSSKGEENLBDLGNQTKO1VERKACTTP1ISN	1320
Qy	1320	TSQONFYTQSRKALKQFRPLPEETELEKRI1YVDDTSTOWSKNKNLTPSTLQIDYNEK	1379
Dp	1321	TSQONFYTQSRKALKQFRPLPEETELEKRI1YVDDTSTOWSKNKNLTPSTLQIDYNEK	1380
Qy	1380	EKGATIOSP1SDCLTSHS1IPANRSP1PAKXSPSP1RPT1YLRVLPODNSHLP1PAS	1439
Dp	1381	EKGATIOSP1SDCLTSHS1IPANRSP1PAKXSPSP1RPT1YLRVLPODNSHLP1PAS	1440
Qy	1440	YRKDSDGOVSSHFLDQAKANNLSL1LTLEMTGDOREVSLGTSATIN5TYKVENYVL	1499
Dp	1441	YRKDSDGOVSSHFLDQAKANNLSL1LTLEMTGDOREVSLGTSATIN5TYKVENYVL	1500
Qy	1500	PKPDLPTSKRVLL1PKVH1YOKDLPFTETSN5SPGHDL1VSGSLDGTGAL1KKNMEANR	1559
Dp	1501	PKPDLPTSKRVLL1PKVH1YOKDLPFTETSN5SPGHDL1VSGSLDGTGAL1KKNMEANR	1560
Qy	1560	PKKVPPLRVYTESASATPEK1LDLP1LAMDNIHYGQ1PKREKMSOKEKSPKPAFKKOTIIS	1619
Dp	1561	PKKVPPLRVYTESASATPEK1LDLP1LAMDNIHYGQ1PKREKMSOKEKSPKPAFKKOTIIS	1620
Qy	1620	LNACESNH1A1AINBQNKPELEVTYMAKOGFTRCLCSQNPYLRKHORREITRTTLOSDOE	1679
Dp	1621	LNACESNH1A1AINBQNKPELEVTYMAKOGFTRCLCSQNPYLRKHORREITRTTLOSDOE	1680
Qy	1680	EL1DDYDRT1SVMKKEDEF1YUDEDENQ5BFOKTRKHNY1IAVERLMDYCMSSP1VLN	1733
Dp	1681	EL1DDYDRT1SVMKKEDEF1YUDEDENQ5BFOKTRKHNY1IAVERLMDYCMSSP1VLN	1740
Qy	1740	RAOSQVPOKRVVPOPEFDG5FTQPL1RBLNBNHGLLGPT1RAVEVDNIWTFPNQMS	1799
Dp	1741	RAOSQVPOKRVVPOPEFDG5FTQPL1RBLNBNHGLLGPT1RAVEVDNIWTFPNQMS	1800
Qy	1800	RYSTYSSL1SYEDDOROGAEPRKNFYKPNETTYTKWQVQHNMA7TKDFEDCKAMAYESD	1859
Dp	1801	RYSTYSSL1SYEDDOROGAEPRKNFYKPNETTYTKWQVQHNMA7TKDFEDCKAMAYESD	1860

Qy	1860	VDEKDVHSLGTLGGLNCHTNTLMPARGQVYQVQEPALFTPIPETKSWYEFEMNRNR	1919
Db	1861	VDLEKDVHSLGTLGGLNCHTNTLMPARGQVYQVQEPALFTPIPETKSWYEFEMNRNR	1920
Qy	1920	APCNIONMEDPTFKENYRFAHINGYIMDTLPGLVMAQDRIHMYLLSMGSENHISHSFG	1979
Db	1921	APCNIONMEDPTFKENYRFAHINGYIMDTLPGLVMAQDRIHMYLLSMGSENHISHSFG	1980
Qy	1980	HVFTYRKKEEYKALVNLPGVFEFVEMLPKSKGIMRVBCLIGELHAGKSTLFLVYSNK	2039
Db	1981	HVFTYRKKEEYKALVNLPGVFEFVEMLPKSKGIMRVBCLIGELHAGKSTLFLVYSNK	2040
Qy	2040	CQTPLGMAASGHIDPQITASGQYGMAPKTLARLHSGSINMASTKEPFSWIKVDLAPMI	2099
Db	2041	CQTPLGMAASGHIDPQITASGQYGMAPKTLARLHSGSINMASTKEPFSWIKVDLAPMI	2100
Qy	2100	IHGIKTQGAQRKSSSLYISQFIWMSLDGKKMQFTYGCNSTGTLWVFGVNDSSGIIKHNF	2159
Db	2101	IHGIKTQGAQRKSSSLYISQFIWMSLDGKKMQFTYGCNSTGTLWVFGVNDSSGIIKHNF	2160
Qy	2160	NPPIIARIYLIHPTHSYNSITSLRMLMGCDLNCSSMPGLMESKALSDAQTASSYTNMF	2219
Db	2161	NPPIIARIYLIHPTHSYNSITSLRMLMGCDLNCSSMPGLMESKALSDAQTASSYTNMF	2220
Qy	2220	ATWSPSKARLHLGGRSNAMRPQVNNPKREMLQVDFOKTKMYGVTTQGVKSLTSMYVKEF	2279
Db	2221	ATWSPSKARLHLGGRSNAMRPQVNNPKREMLQVDFOKTKMYGVTTQGVKSLTSMYVKEF	2280
Qy	2280	LTSSSQDGHQWTLFPNGKVKYKFGQNDSPFPVYVNSLDPLLTFLRLRIHPQSWVHQAIR	2339
Db	2281	LTSSSQDGHQWTLFPNGKVKYKFGQNDSPFPVYVNSLDPLLTFLRLRIHPQSWVHQAIR	2340
Qy	2340	MEVLGCEAKODLY 2351	
Db	2341	MEVLGCEAKODLY 2352	
RESULT 75			
ID	AAAM1352		
AAAM1352	standard; Protein; 2351 AA.		
XX	AAAM1352;		
AC			
XX	17-NOV-1997	(first entry)	
DT			
XX			
DE	Active Factor VIII:C analogue C248X.		
XX			
KW	Factor VIII:C; analogue; glycoprotein; blood coagulation cascade; fibrinogen; fibrin clot; hemostasis; haemophilia A; bleeding diathesis; plasma protease; thrombin; immunogen; antibody; haemophilic; therapy; proteolytic cleavage.		
KW			
KW			
XX	Homo sapiens.		
OS	Synthetic.		
XX			
XX			
FH	Key	Location/Qualifiers	
FT	Peptide	1..19	
FT		/note= "signal peptide"	
FT	Protein	20..2351	
FT		/note= "mature Factor VIII:C"	
FT	Region	20..1667	
FT		/note= "heavy chain fragment"	
FT	Modified-site	267	
FT		/label= Phe, Glu, Pro	
FT	Region	1668..2350	
FT		/note= "light chain fragment"	
FT	Domain	760..1667	
FT		/note= "B domain"	
XX	WO9703195-A1.		
PN			
XX			
PD	30-JAN-1997.		
XX			

PF 09-JUL-1996; 96WO-US11444.  
XX  
PR 11-JUL-1995; 95US-0001025.  
PA (CHIR ) CHIRON CORP.  
XX  
PI Cohen FE, Hung DT, Innis M;  
DR WPI: 1997-119050/11.  
PT Factor VIII:C analog modified adjacent to a non-activating Arg  
residue - used in the treatment of haemophilias, by improvement of  
hemostasis  
XX  
PS Claim 12: Page -: 90pp: English.  
XX  
CC AAM1330-W11472 represent active Factor VIII:C analogues of the  
invention. These sequences were created by mutating the wild type Factor  
VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
analogues comprise a native Factor VIII:C polypeptide modified at a site  
adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
dipeptide is created. Factor VIII:C is a large glycoprotein that  
participates in the blood coagulation cascade that ultimately converts  
soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
activated by plasma proteases, such as thrombin. During activation the  
mature polypeptide is cleaved to generate heavy and light chain fragments  
that are further cleaved. Complexes of two or more of the analogues,  
nucleic acids and vectors encoding them may be used alone or in  
conjunction with each other, for the prevention or treatment of active  
Factor VIII:C deficiency in a mammal. The analogues may be used as  
immunogens to raise antibodies, and in the treatment of haemophilias, by  
improvement of haemostasis. The analogues are resistant to proteolytic  
cleavage and display increased plasma half-life. They may be administered  
at lower dosages and by different modes of administration.  
XX  
SQ Sequence 2351 AA:  
Query Match 99.9%; Score 12407; DB 18; Length 2351.  
Best Local Similarity 100.0%; Prid. No. 0;  
Matches 2350; Conservative 0; Mismatches 1; Indels 0; Gaps 0;  
QY 1 MQTELSTCFCLLRFCSATRRYYLGAVELSMWYQSDGLGELPYDARFPPRPKSPFN 60  
DB 1 MQTELSTCFCLLRFCSATRRYYLGAVELSMWYQSDGLGELPYDARFPPRPKSPFN 60  
QY 61 TSVVYKKTLEFVEFTDHLFNIAKPPPMGLGPTIOAEYDTVVITLKNMASHPVSLHAY 120  
DB 61 TSVVYKKTLEFVEFTDHLFNIAKPPPMGLGPTIOAEYDTVVITLKNMASHPVSLHAY 120  
QY 121 GVSVMKASGAEYDDQTSQREKEDKVFPGSHTTYWVYLVKENGPMASDPLCLTYSLSH 180  
DB 121 GVSVMKASGAEYDDQTSQREKEDKVFPGSHTTYWVYLVKENGPMASDPLCLTYSLSH 180  
QY 181 VDLVKDNLNSGLIGALLVCREGSLAKEKOTLHFFILFAVPEGSKSMSEKNSLMDRD 240  
DB 181 VDLVKDNLNSGLIGALLVCREGSLAKEKOTLHFFILFAVPEGSKSMSEKNSLMDRD 240  
QY 241 AASARAMPKMTVNGVYVNSLPLGLIGCHRRSVYWHVIGCTTPEVHSLFELGHFTLVNRH 300  
DB 241 AASARAMPKMTVNGVYVNSLPLGLIGCHRRSVYWHVIGCTTPEVHSLFELGHFTLVNRH 300  
QY 301 ROASLELSNTEFLTQTLMDLGOFLFCHISSHODGMEAVYKVDSCPEPQRMKNNE 360  
DB 301 ROASLELSNTEFLTQTLMDLGOFLFCHISSHODGMEAVYKVDSCPEPQRMKNNE 360  
QY 361 EAEYDDDLTDSMDVYRFDDNSPFTQIRSAKAKPTWVHYIAAEEEDMDAPLVLA 420  
DB 361 EAEYDDDLTDSMDVYRFDDNSPFTQIRSAKAKPTWVHYIAAEEEDMDAPLVLA 420  
QY 421 PDDRSKSYQLNNGPQIRIGRKYKKVRFMAATDETFTKTRALIOHESGILGLPYGEVDTL 480  
DB 421 PDDRSKSYQLNNGPQIRIGRKYKKVRFMAATDETFTKTRALIOHESGILGLPYGEVDTL 480

DB 421 PDDRSKSYQLNNGPQIRIGRKYKKVRFMAATDETFTKTRALIOHESGILGLPYGEVDTL 480  
QY 481 LIIFKQASRPYNIYPHGITDVPRELYSRRLPKGVKHLKDPILPGEITFKIKWYVEDGP 540  
DB 481 LIIFKQASRPYNIYPHGITDVPRELYSRRLPKGVKHLKDPILPGEITFKIKWYVEDGP 540  
QY 541 TKGDPRCLTRYRYSFVNMERDLASGLIGPLLCYKESVQQRNQIMSDKRWVILFVFE 600  
DB 541 TKGDPRCLTRYRYSFVNMERDLASGLIGPLLCYKESVQQRNQIMSDKRWVILFVFE 600  
QY 601 NRSWYLTENIQRLPNPAGVQLEDPPEQASNTWASTNGVYFPSQLSLCYLAEVAYWYIS 660  
DB 601 NRSWYLTENIQRLPNPAGVQLEDPPEQASNTWASTNGVYFPSQLSLCYLAEVAYWYIS 660  
QY 661 IGAOTDFLAFYFSGYTFKHKWYEDTLTLPFSGETVFMNENPGLMILGCHNSDFNRNG 720  
DB 661 IGAOTDFLAFYFSGYTFKHKWYEDTLTLPFSGETVFMNENPGLMILGCHNSDFNRNG 720  
QY 721 MTALLKVSQDKMTGDIYEDSYEDISAYLLSKNNALIEPFSQNSRHPSTRQOFNATTI 780  
DB 721 MTALLKVSQDKMTGDIYEDSYEDISAYLLSKNNALIEPFSQNSRHPSTRQOFNATTI 780  
QY 781 PENDIEKTPWFHARTPMKIQIOWSSDLMMLROSPTRHGLSLDLOEARYETFSDDPS 840  
DB 781 PENDIEKTPWFHARTPMKIQIOWSSDLMMLROSPTRHGLSLDLOEARYETFSDDPS 840  
QY 841 PGALDSNNSISEMTHTRPOLHNSGDMWTPESGLOLRNDEKLGTTAATELKKIDPFKYST 900  
DB 841 PGALDSNNSISEMTHTRPOLHNSGDMWTPESGLOLRNDEKLGTTAATELKKIDPFKYST 900  
QY 901 SNNLITRIPSDNLAAQDNTSSIGPPSNPVHYDSQDLTTLFGKSSPLTESGGLSLSEE 960  
DB 901 SNNLITRIPSDNLAAQDNTSSIGPPSNPVHYDSQDLTTLFGKSSPLTESGGLSLSEE 960  
QY 961 NNDKSLLESLMSQSSSGKRVSTESGELFKGRRAHGALITKONALFKYSISLKTN 1020  
DB 961 NNDKSLLESLMSQSSSGKRVSTESGELFKGRRAHGALITKONALFKYSISLKTN 1020  
QY 1021 KTSNNSATNRKTHIDPSSLILENSPVMONILESDETEKVTPLIHDRMLDKNATRLRL 1080  
DB 1021 KTSNNSATNRKTHIDPSSLILENSPVMONILESDETEKVTPLIHDRMLDKNATRLRL 1080  
QY 1081 NMSKTKTSSKNMEMYQOKKEGPIPPDQNDPMGFMLFLPESARMIORTGKNSLNSG 1140  
DB 1081 NMSKTKTSSKNMEMYQOKKEGPIPPDQNDPMGFMLFLPESARMIORTGKNSLNSG 1140  
QY 1141 QGSPFKOLVSLGPEKSYEGONFLSEKNVYVKGELTKDGLKEMVFPSSRNLFITLNDN 1200  
DB 1141 QGSPFKOLVSLGPEKSYEGONFLSEKNVYVKGELTKDGLKEMVFPSSRNLFITLNDN 1200  
QY 1201 LHENNTHOEKKIOEIELEKETLQIENVVLPOIHTVGTAKNFKNLFLSTLQONVGSYD 1260  
DB 1201 LHENNTHOEKKIOEIELEKETLQIENVVLPOIHTVGTAKNFKNLFLSTLQONVGSYD 1260  
QY 1261 GAYAVLQDERSLNDSTNRKTKHTAFSKGEBENLEGLOKQIVEXYACTTGISNT 1320  
DB 1261 GAYAVLQDERSLNDSTNRKTKHTAFSKGEBENLEGLOKQIVEXYACTTGISNT 1320  
QY 1321 SOQNFVTOQRKRALKOPRLPLETELEKRIIYDDTSTOWSKNNKHLTPSTLIQIDYNEKE 1380  
DB 1321 SOQNFVTOQRKRALKOPRLPLETELEKRIIYDDTSTOWSKNNKHLTPSTLIQIDYNEKE 1380  
QY 1381 KGATQSPSLDCLTRSHSIPQANRSPPLAKVSSPSTIRPYLTRVLFDONSSHLPASYS 1440  
DB 1381 KGATQSPSLDCLTRSHSIPQANRSPPLAKVSSPSTIRPYLTRVLFDONSSHLPASYS 1440  
QY 1441 RKKDSGVESHPLQAGAKKNNLSLALITLLEMTGDQREVGSIGTSATNSVYKRVENTVLP 1500  
DB 1441 RKKDSGVESHPLQAGAKKNNLSLALITLLEMTGDQREVGSIGTSATNSVYKRVENTVLP 1500  
QY 1501 KFDLPKTSQKVELLPKHVITQKRLPFTETSNQSPCHLDIVGSLDGTGATKMNENARP 1560  
DB 1501 KFDLPKTSQKVELLPKHVITQKRLPFTETSNQSPCHLDIVGSLDGTGATKMNENARP 1560



QY	1561	IKVPELVNAPAESAKTPSKLLIDPLAMNNHNGOIRKEEMKSOEKSPEKTAFFKKDTIISL	1620
Db	1561	GKPEPLNVAESSAKTPSKLLIDPLAMNNHNGIPIREEMKSOEKSPEKTAFFKKDTIISL	1620
QY	1621	NACSNHAIALINEGONKPELVTWAKOFTERLCSQNPVYLKRNOREITFTLLSDOE	1680
Db	1621	NACSNHAIALINEGONKPELVTWAKOFTERLCSQNPVYLKRNOREITFTLLSDOE	1680
QY	1681	IDYDDTISVEMKKEDEPDIDEDENOSRSPFOKKTIRHYEIAAVERLMDYGMSSPHYLBNR	1740
Db	1681	IDYDDTISVEMKKEDEPDIDEDENOSRSPFOKKTIRHYEIAAVERLMDYGMSSPHYLBNR	1740
QY	1741	AQSGSVQFQKVVYQFETGSGFTQPLVRCGLNHLGLLGLPYIRAEVEDNIMWTFRMOASR	1800
Db	1741	AQSGSVQFQKVVYQFETGSGFTQPLVRCGLNHLGLLGLPYIRAEVEDNIMWTFRMOASR	1800
QY	1801	PVSFSSLSIYEEDQOQGAEPKKNFVNPNETKTYEMKVOHNHAPLTKDEPFCKKMAAFSDV	1860
Db	1801	PVSFSSLSIYEEDQOQGAEPKKNFVNPNETKTYEMKVOHNHAPLTKDEPFCKKMAAFSDV	1860
QY	1861	DEKDVHSGILGVLVCHNTLNPANHROVTQOERLAFETTFDEKTSWYTEMERNCR	1920
Db	1861	DEKDVHSGILGVLVCHNTLNPANHROVTQOERLAFETTFDEKTSWYTEMERNCR	1920
QY	1921	PONTOMEDPTFKKNYFNFAINGYIMDTLPGLVNAODORIRMTLLSMGSNENHSHFESG	1980
Db	1921	PONTOMEDPTFKKNYFNFAINGYIMDTLPGLVNAODORIRMTLLSMGSNENHSHFESG	1980
QY	1981	VETVARKKEEKMALYNLVYGVFEVEMLPKAGIMWRECLLGEHILHAGMSTLEFLVYSNKC	2040
Db	1981	VETVARKKEEKMALYNLVYGVFEVEMLPKAGIMWRECLLGEHILHAGMSTLEFLVYSNKC	2040
QY	2041	QTPGLMASGHIRFOITTAAGYQGWAPKRLARLHSGSINAMSTKEPESWIKVLLAPMI	2100
Db	2041	QTPGLMASGHIRFOITTAAGYQGWAPKRLARLHSGSINAMSTKEPESWIKVLLAPMI	2100
QY	2101	HSIKTKQGRQKFSKLTISQFIIMYSLQGGKMOYRBNSTNGTLMFPNGVSSGIRKINIFN	2160
Db	2101	HSIKTKQGRQKFSKLTISQFIIMYSLQGGKMOYRBNSTNGTLMFPNGVSSGIRKINIFN	2160
QY	2161	PIRTAIRYLPHHYISIRSTLMELMGCDLNSGSMPLGSHESKALISDQITASSYFNHMA	2220
Db	2161	PIRTAIRYLPHHYISIRSTLMELMGCDLNSGSMPLGSHESKALISDQITASSYFNHMA	2220
QY	2221	TMSPEKARHLQGRSNAAMPVONNPKEMLOYDQKTMKATGVTQGVKSLTISMYKEFL	2280
Db	2221	TMSPEKARHLQGRSNAAMPVONNPKEMLOYDQKTMKATGVTQGVKSLTISMYKEFL	2280
QY	2281	ISSSDQGHQWTLFFQNGKVKVFGQNDQSFPPVYNSIDPELRLRYLRIHPQSWHQAIALRM	2340
Db	2281	ISSSDQGHQWTLFFQNGKVKVFGQNDQSFPPVYNSIDPELRLRYLRIHPQSWHQAIALRM	2340
QY	2341	EVLGCEADQDLY 2351	
Db	2341	EVLGCEADQDLY 2351	
RESULT 76			
ID	AAAM11468		
AC	AAAM11468	standard; Protein; 2351 AA.	
XX	AAAM11468:		
DT	21-NOV-1997	(first entry)	
XX	Active Factor VIII:C analogue, delta 1720, + residue 1719 insertion.		
XX	Factor VIII:C analogue; glycoprotein; blood coagulation cascade;		
KM	fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;		
KM	plasma protease; chrombin; immunogen; antibody; haemophilic; therapy;		
XX	proteolytic cleavage.		

OS	Homo sapiens.
XX	Synthetic.
FT	key
FT	Peptide
FT	/note= "signal peptide"
FT	20..2351
FT	Protein
FT	/note= "mature Factor VIII:C"
FT	20..1667
FT	Region
FT	/note= "heavy chain fragment"
FT	1668..2350
FT	Region
FT	/note= "light chain fragment"
FT	760..1667
FT	Domain
FT	/note= "B domain"
FT	1738
FT	Modified site
FT	/label= Phe, Glu, Pro
FT	/note= "inserted residue"
FT	Misc-difference
FT	1739..1740
FT	/note= "site of 1 residue deletion"
XX	
PN	MO9703195-A1.
XX	
PD	30-JAN-1997.
PF	
PF	09-JUL-1996; 96WO-US11444.
PR	
PR	11-JUL-1995; 95US-0001025.
PA	(CHIR ) CHIRON CORP.
XX	
PI	Cohen FE, Hung DT, Innis M;
XX	
DR	WPI: 1997-119050/11.
PT	
PT	Factor VIII:C analog modified adjacent to a non-activating Arg
PT	residue - used in the treatment of haemophilias, by improvement of
PT	haemostasis
XX	
XX	
XX	Claim 38; Page -: 90pp; English.
CC	
CC	AAM11330-W11472 represent active Factor VIII:C analogues of the
CC	invention. These sequences were created by mutating the wild type Factor
CC	VIII:C coding sequence (see AAV5157) using mutagenic primers. The
CC	analogues comprise a native Factor VIII:C polypeptide modified at a site
CC	adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC	dipeptide is created. Factor VIII:C is a large glycoprotein that
CC	participates in the blood coagulation cascade that ultimately converts
CC	soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC	deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC	X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC	activated by plasma proteases, such as thrombin. During activation the
CC	mature polypeptide is cleaved to generate heavy and light chain fragments
CC	that are further cleaved. Complexes of two or more of the analogues,
CC	nucleic acids and vectors encoding them may be used alone or in
CC	conjunction with each other, for the prevention or treatment of active
CC	Factor VIII:C deficiency in a mammal. The analogues may be used as
CC	immunogens to raise antibodies, and in the treatment of haemophilias, by
CC	improvement of haemostasis. The analogues are resistant to proteolytic
CC	cleavage and display increased plasma half-life. They may be administered
CC	at lower dosages and by different modes of administration.
XX	
SQ	Sequence
XX	2351 AA:
Query Match	99.98; Score 12406; DB 18; Length 2351;
Best Local Similarity	99.98; Pctd No. 0;
Matches 2349; Conservative	0; Mismatches 2; Indels 0; Gaps 0;
OY	1 MO1E1STCFCLLRCEFSATRRYYLGAVELSWDYMQSDLGELPYDANFPPRPKSPFN 60
DB	I MO1E1STCFCLLRCEFSATRRYYLGAVELSWDYMQSDLGELPYDANFPPRPKSPFN 60
OY	TSVYVKKTLEVFETDHLFNIAKRPMNGLLGPTIQAEEVDVTITLKNAASHPSLAIV 120

Db 61 TSVYKKTLEVEETDHLFNIAKPRPPMGLIGPTIOAEVYDVIYVTLKNAHSHPVSLHAY 120  
Qy 121 GVSYWKASSEGAEYDDOTSOREKEDDKVPPGGSHYVWOLKENGPMASDPLCLTYSLSH 180  
Db 121 GVSYWKASSEGAEYDDOTSOREKEDDKVPPGGSHYVWOLKENGPMASDPLCLTYSLSH 180  
Qy 181 VDLVKDNLMSGLIGALLVCREGSLAKEKTOJLHKFTLLFANFDEGKSMHSETKNSLMODRD 240  
Db 181 VDLVKDNLMSGLIGALLVCREGSLAKEKTOJLHKFTLLFANFDEGKSMHSETKNSLMODRD 240  
Qy 241 AASARAMPKMHYVNGVYNNSLPGLIGCHRSYVHWJTGKCTPEVHSTFLBGHFTLYRNH 300  
Db 241 AASARAMPKMHYVNGVYNNSLPGLIGCHRSYVHWJTGKCTPEVHSTFLBGHFTLYRNH 300  
Qy 301 ROASLEISPIITFLAOTLLMDGOFLLFCHSHSHOHDMGEAVYKVDSCEEPOLRMKNNE 360  
Db 301 ROASLEISPIITFLAOTLLMDGOFLLFCHSHSHOHDMGEAVYKVDSCEEPOLRMKNNE 360  
Qy 361 EAEYDDDLTDSEMDVYRFDNDSNPSFIOIRSVAKKHAKTWHYHTAAEEDMDYAPLYLA 420  
Db 361 EAEYDDDLTDSEMDVYRFDNDSNPSFIOIRSVAKKHAKTWHYHTAAEEDMDYAPLYLA 420  
Qy 421 PDDRSYKSQYLNNGPORIGKTKKVRMAAYDETFTKREAIQHESGILGPLYGEGDYL 480  
Db 421 PDDRSYKSQYLNNGPORIGKTKKVRMAAYDETFTKREAIQHESGILGPLYGEGDYL 480  
Qy 481 LIIIFKNOASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDPILPGEIFPKYKMYVEDGP 540  
Db 481 LIIIFKNOASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDPILPGEIFPKYKMYVEDGP 540  
Qy 541 TKSOPRCLTRYSSAFNMERDLASGLITPLICYKESVOGRQOIMSKRNVILFVDFE 600  
Db 541 TKSOPRCLTRYSSAFNMERDLASGLITPLICYKESVOGRQOIMSKRNVILFVDFE 600  
Qy 601 NRSWLTENIORLPLNPAGVOLEDEPQASNIMHSINGVFSLOLSYCLHEVAWYILS 660  
Db 601 NRSWLTENIORLPLNPAGVOLEDEPQASNIMHSINGVFSLOLSYCLHEVAWYILS 660  
Qy 661 IGAQTDPLSAVFSGYTFKHKMYEDTLTPFSGSETVFMSEMPGIMLIGCNSDFNRG 720  
Db 661 IGAQTDPLSAVFSGYTFKHKMYEDTLTPFSGSETVFMSEMPGIMLIGCNSDFNRG 720  
Qy 721 WTALIKVSSCDKNGYVEDSYEDISAYLLSKNAITPRSFONSHPSTROKOPNATTI 780  
Db 721 WTALIKVSSCDKNGYVEDSYEDISAYLLSKNAITPRSFONSHPSTROKOPNATTI 780  
Qy 781 PENDIEKTDWFAHRTPMKPIQNVSSDLMMLRQSPTRPGLSLSDLOEAKYETFSDDPS 840  
Db 781 PENDIEKTDWFAHRTPMKPIQNVSSDLMMLRQSPTRPGLSLSDLOEAKYETFSDDPS 840  
Qy 841 PGALDSNNSLSEMTHERPOLHHSGDMVTPESGLQLRINKELGTATATELKLDPKVSST 900  
Db 841 PGALDSNNSLSEMTHERPOLHHSGDMVTPESGLQLRINKELGTATATELKLDPKVSST 900  
Qy 901 SNMLISTIPSDNLAAGDNTSSIGPSPMYHYDSDLTTLFGKSSPLTESGPISTSEE 960  
Db 901 SNMLISTIPSDNLAAGDNTSSIGPSPMYHYDSDLTTLFGKSSPLTESGPISTSEE 960  
Qy 961 NNDSKLLESGIAMSQESSGKNVSTSESGRLFCKGRAHPALLTKDNALFKVYSISLLKTN 1020  
Db 961 NNDSKLLESGIAMSQESSGKNVSTSESGRLFCKGRAHPALLTKDNALFKVYSISLLKTN 1020  
Qy 1021 KTSNNSATNRKTHDGSLLIENSPSYWONLTLEDTEFFKVPLJHJDRMLDKNAATLRL 1080  
Db 1021 KTSNNSATNRKTHDGSLLIENSPSYWONLTLEDTEFFKVPLJHJDRMLDKNAATLRL 1080  
Qy 1081 NMSNKTTSKKNEMAYOQKKEGPIPPDAONPDMSGFFKMLFLPESARWIORTHGKNSLNSG 1140  
Db 1081 NMSNKTTSKKNEMAYOQKKEGPIPPDAONPDMSGFFKMLFLPESARWIORTHGKNSLNSG 1140  
Qy 1141 OGSPSKOLVSLGPEKSVYEGONFLSEKKNVYVVGKEEFTKDVGLKEWFPSSRNLFTJNLN 1200  
Db 1141 OGSPSKOLVSLGPEKSVYEGONFLSEKKNVYVVGKEEFTKDVGLKEWFPSSRNLFTJNLN 1200

Qy 1201 LHENNTNHOEKKIOEBIEKRETLLOENVVLPQJHVTYGTKNFMKMLFLLSRQNVESGSD 1260  
Db 1201 LHENNTNHOEKKIOEBIEKRETLLOENVVLPQJHVTYGTKNFMKMLFLLSRQNVESGSD 1260  
Qy 1261 GAYAPVLQDPRSLNDSTNRTKHTAHFSKGOEENLEGLOKQOIVEKYACTYRISPNT 1320  
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Qy 1321 SQONFYQSRKRALKQFRLPELETLEKRIIYDDTSTQNSKMMKLTJSTLOTIDYNEK 1380  
Db 1321 SQONFYQSRKRALKQFRLPELETLEKRIIYDDTSTQNSKMMKLTJSTLOTIDYNEK 1380  
Qy 1381 KGATQSPFLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYTLFVLEFQDNSSHLPAASY 1440  
Db 1381 KGATQSPFLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYTLFVLEFQDNSSHLPAASY 1440  
Qy 1441 RKKSQVOESSHFLQAKKNNLSLAILTLEMTGDPORVGSLOTSATNSVTYKKYENTVLP 1500  
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Qy 1501 KPDLKTSKVEILLPVVHYLOKFLPETTSNGSPGHLDBESLLQGTREGAIKKNENNR 1560  
Db 1501 KPDLKTSKVEILLPVVHYLOKFLPETTSNGSPGHLDBESLLQGTREGAIKKNENNR 1560  
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Qy 1621 NACESNHAIAINEGONKPEIETVAKOGREBLCSQNPVYLKRHQREITRTTLOSPOE 1680  
Db 1621 NACESNHAIAINEGONKPEIETVAKOGREBLCSQNPVYLKRHQREITRTTLOSPOE 1680  
Qy 1681 IDYDDTISVEKKEDFDIYDEBENOSPSPSKTRHFLAAERLMDVGMSSSHVLYXRP 1740  
Db 1681 IDYDDTISVEKKEDFDIYDEBENOSPSPSKTRHFLAAERLMDVGMSSSHVLYXRP 1740  
Qy 1741 AOSGSVPQFKVYFOEFTDGSFTQPLYRGEINELHGLSPYIRAEVDNIMVYPRNOAS 1800  
Db 1741 AOSGSVPQFKVYFOEFTDGSFTQPLYRGEINELHGLSPYIRAEVDNIMVYPRNOAS 1800  
Qy 1801 PYSFSSLSYEEBDOGAEPKRNKVRKNEKTYFMKVYOHNAAPKDFDCKAAYRSOV 1860  
Db 1801 PYSFSSLSYEEBDOGAEPKRNKVRKNEKTYFMKVYOHNAAPKDFDCKAAYRSOV 1860  
Qy 1861 DLEKDVHSGILGPLYCHNTNLNPAHSGQVTVQEPALFTTIDETKSWYFTEMMERNCR 1920  
Db 1861 DLEKDVHSGILGPLYCHNTNLNPAHSGQVTVQEPALFTTIDETKSWYFTEMMERNCR 1920  
Qy 1921 PCNTQMEDPTEFKENYRFAHNGYIMDTLPGLVMAODORIHWYLLSMGSENENHSIHPSGH 1980  
Db 1921 PCNTQMEDPTEFKENYRFAHNGYIMDTLPGLVMAODORIHWYLLSMGSENENHSIHPSGH 1980  
Qy 1981 VFTYRKKEEYKMLVLYLPGVEYETEMLPKSAAGIWRRECEJIEHHAAMSTLFLVYSNKC 2040  
Db 1981 VFTYRKKEEYKMLVLYLPGVEYETEMLPKSAAGIWRRECEJIEHHAAMSTLFLVYSNKC 2040  
Qy 2041 QTPJGMASSHIRDPQITASGOYGOMAPKLARLHSSGINASTKEPESWIKVLDLAPMII 2100  
Db 2041 QTPJGMASSHIRDPQITASGOYGOMAPKLARLHSSGINASTKEPESWIKVLDLAPMII 2100  
Qy 2101 HGKTOGARQFSSLSISOFIIMYSLODKMQYVRGNSGTGLMVFEGVWDSGKIHNFN 2160  
Db 2101 HGKTOGARQFSSLSISOFIIMYSLODKMQYVRGNSGTGLMVFEGVWDSGKIHNFN 2160  
Qy 2161 PPIIARIRLHPHYISIRBSTLMELMGCDLSSCMPLGEKSAISDAOITASVFTMFA 2220  
Db 2161 PPIIARIRLHPHYISIRBSTLMELMGCDLSSCMPLGEKSAISDAOITASVFTMFA 2220  
Qy 2221 TWSPSKARLHLQGRSNAAMPQVNNPKEMVLQVDFOKTMYKYVTTQGVKSLTSMYKEFL 2280  
Db 2221 TWSPSKARLHLQGRSNAAMPQVNNPKEMVLQVDFOKTMYKYVTTQGVKSLTSMYKEFL 2280

OY 2281 ISSQDGHQWTLFPQNGKVKVPGQNGDSFPPVNSLDPPLLRRLRRIHPHOSWQIALRM 2340  
|||||  
DB 2281 ISSQDGHQWTLFPQNGKVKVPGQNGDSFPPVNSLDPPLLRRLRRIHPHOSWQIALRM 2340  
OY 2341 EYLGCENADLY 2351  
|||||  
DB 2341 EYLGCENADLY 2351  
RESULT 77  
AAW11377  
ID AAW11377 standard; Protein; 2351 AA.  
XX  
AC AAW11377;  
DX 18-NOV-1997 (first entry)  
XX  
DE Active Factor VIII:C analogue, delta 335, + residue 334 insertion.  
XX  
KM Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;  
KM fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KM plasma protease; thrombin; immunogen; antibody; haemophilia; therapy;  
KM proteolytic cleavage.  
OS Homo sapiens.  
OS Synthetic.  
FH Key  
FH Peptide  
FT /note="signal peptide"  
FT 20..2351  
FT /note="mature Factor VIII:C"  
FT 20..1667  
FT Region  
FT /note="heavy chain fragment"  
FT 353  
FT Modified-site  
FT /label="Phe, Glu, Pro  
FT /note="inserted residue"  
FT MISC-difference 354..355  
FT /note="site of 1 residue deletion"  
FT Region  
FT 1668..2350  
FT /note="light chain fragment"  
FT 760..1667  
FT Domain  
FT /note="B domain"  
XX  
XX MO9703195-A1.  
XX  
XX PD 30-JAN-1997.  
XX  
XX PF 09-JUL-1996; 96WO-US11444.  
XX  
XX PR 11-JUL-1995; 95US-0001025.  
XX  
XX PA (CHIR ) CHIRON CORP.  
XX  
XX PI Cohen FE, Hung DT, Innis M;  
XX  
XX DR WPI; 1997-119050/11.  
XX  
XX Factor VIII:C analog modified adjacent to a non-activating Arg  
XX residue - used in the treatment of haemophiliacs, by improvement of  
XX haemostasis  
XX  
XX PS Claim 18; Page -: 90pp; English.  
XX  
XX CC AAW11330-W11472 represent active Factor VIII:C analogues of the  
XX invention. These sequences were created by mutating the wild type Factor  
XX VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
XX analogues comprise a native Factor VIII:C polypeptide modified at a site  
XX adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
XX dipeptide is created. Factor VIII:C is a large glycoprotein that  
XX participates in the blood coagulation cascade that ultimately converts  
XX soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
XX deficiency in Factor VIII:C is responsible for haemophilia A, which is an

CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophiliacs, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX  
XX Sequence 2351 AA:  
SO  
Query Match 99.9%; Score 12406; DB 18; Length 2351;  
Best Local Similarity 99.9%; Pred. No. 0;  
Matches 2349; Conservative 0; Mismatches 2; Indels 0; Gaps 0;  
OY 1 MOIELSTCFELCLRLRCFSATRRYYLAGVELSMDYMQSDLGELPVDAREPPRVKSPFPN 60  
DB 1 MOIELSTCFELCLRLRCFSATRRYYLAGVELSMDYMQSDLGELPVDAREPPRVKSPFPN 60  
OY 61 TSVYKKTLPEFTDHLFNIAKPRPPMGLGPTIQAEVYDVITLKMASHPSLHAY 120  
DB 61 TSVYKKTLPEFTDHLFNIAKPRPPMGLGPTIQAEVYDVITLKMASHPSLHAY 120  
OY 121 GSVYKASEGAEYDDOTSOREKEDDKVEPGGSHYVMOVLKENGPMASDPLCLTYSLSH 180  
DB 121 GSVYKASEGAEYDDOTSOREKEDDKVEPGGSHYVMOVLKENGPMASDPLCLTYSLSH 180  
OY 181 VDLVKDLNSGLIGALLVCRGSLAKKEKTQTLHKFLLFAVFDGKSMHSETKNSLMODRD 240  
DB 181 VDLVKDLNSGLIGALLVCRGSLAKKEKTQTLHKFLLFAVFDGKSMHSETKNSLMODRD 240  
OY 241 AASARAPKMTVNGVYNSGLIGCRKRSVYHVGKTPREVSITLREHPFLVNH 300  
DB 241 AASARAPKMTVNGVYNSGLIGCRKRSVYHVGKTPREVSITLREHPFLVNH 300  
OY 241 AASARAPKMTVNGVYNSGLIGCRKRSVYHVGKTPREVSITLREHPFLVNH 300  
DB 241 AASARAPKMTVNGVYNSGLIGCRKRSVYHVGKTPREVSITLREHPFLVNH 300  
OY 301 ROASLEISPIFTLAOTLLMDLGOFLLCFCHISSHQHGMAYVVDSCPEEPXOKMKNE 360  
DB 301 ROASLEISPIFTLAOTLLMDLGOFLLCFCHISSHQHGMAYVVDSCPEEPXOKMKNE 360  
OY 361 EAEYDDDLTSEMDVYRFDDNSPFIQISVAKKHPTWVHYIAEEEDMDYAPLVLA 420  
DB 361 EAEYDDDLTSEMDVYRFDDNSPFIQISVAKKHPTWVHYIAEEEDMDYAPLVLA 420  
OY 421 PDORSYKQYLNNGPORIGKTKKRYKFAFYADEFTKREALQHESSILGPLYGEGDTL 480  
DB 421 PDORSYKQYLNNGPORIGKTKKRYKFAFYADEFTKREALQHESSILGPLYGEGDTL 480  
OY 481 LIIFFKQASRPYNTYRPGITDVAPLYSRLLRGVYKHLKDEPILPGEIFYKWTYVEDGP 540  
DB 481 LIIFFKQASRPYNTYRPGITDVAPLYSRLLRGVYKHLKDEPILPGEIFYKWTYVEDGP 540  
OY 541 TKSDFRCLTRYSSFFVMEMPDLASGLIGPLLICKRESYDQKQMSDRNIILESYDE 600  
DB 541 TKSDFRCLTRYSSFFVMEMPDLASGLIGPLLICKRESYDQKQMSDRNIILESYDE 600  
OY 601 NRSWLTENIQRFLNPAGVQLEDEPQASINMHSINGVYFDSIQVCLHNAVWYLLS 660  
DB 601 NRSWLTENIQRFLNPAGVQLEDEPQASINMHSINGVYFDSIQVCLHNAVWYLLS 660  
OY 661 ICAQDFLSVFSGYTKHKMYVEDTLFPFSGEYFMSKEMNGMLIIGCNSPFRNRG 720  
DB 661 ICAQDFLSVFSGYTKHKMYVEDTLFPFSGEYFMSKEMNGMLIIGCNSPFRNRG 720  
OY 721 MTALLKVSCKKNGDYEDSYEDISAYILSKNNAIPRFSQNSHPSTROKQFNATTI 780  
DB 721 MTALLKVSCKKNGDYEDSYEDISAYILSKNNAIPRFSQNSHPSTROKQFNATTI 780  
OY 781 PENDIEKTDPMFAHRTMPKIONVSSDMLMLRQSPTPGSLSLQBAKYTFSDPS 840  
DB 781 PENDIEKTDPMFAHRTMPKIONVSSDMLMLRQSPTPGSLSLQBAKYTFSDPS 840

QY 841 PGADSNNSISEMTHPPOLAHSGDMVFTPESCLOLRINEKLTGTTATATLTKLIDFKVSST 900  
DB 841 PGADSNNSISEMTHPPOLAHSGDMVFTPESCLOLRINEKLTGTTATATLTKLIDFKVSST 900  
QY 901 SNNLSTIPSDNLAAGTDNNTSSLGPPSMVHYDSQDLOTTLTGKKSSPTEBSGGSLSEEE 960  
DB 901 SNNLSTIPSDNLAAGTDNNTSSLGPPSMVHYDSQDLOTTLTGKKSSPTEBSGGSLSEEE 960  
QY 961 NNDKSLIESGLMNSOESMGKNVSTESGRLPKGRARAPALLTKDALFKVSIISLTKTN 1020  
DB 961 NNDKSLIESGLMNSOESMGKNVSTESGRLPKGRARAPALLTKDALFKVSIISLTKTN 1020  
QY 1021 KTSNNSATNRKTHIDGFSLLIENSPSWONILLESPTERRKYTPLIHDMRLMDKNATAPL 1080  
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DB 1081 NHRNKTTSKKMMEVOOKKEGPIPPDAONPMKSEFFKMLFPESARMIQRTGKNSLNSG 1140  
QY 1141 QGPPKQOLVSLGPEKSYEGONFLSEKNKYVVGKGEFTKDVGLKEMVPPSSRNFLTNDLN 1200  
DB 1141 QGPPKQOLVSLGPEKSYEGONFLSEKNKYVVGKGEFTKDVGLKEMVPPSSRNFLTNDLN 1200  
QY 1201 LHENNTNHOEKKIOELEKKEKTELLIOENVVLPOIHTVYGTGKNFMKNLELLSTRONVGSYD 1260  
DB 1201 LHENNTNHOEKKIOELEKKEKTELLIOENVVLPOIHTVYGTGKNFMKNLELLSTRONVGSYD 1260  
QY 1261 GAYAPVLODFRSNTNRKTHAHSPKKEEENLEGIAGNOTOYIEKVACTTRISPTM 1320  
DB 1261 GAYAPVLODFRSNTNRKTHAHSPKKEEENLEGIAGNOTOYIEKVACTTRISPTM 1320  
QY 1321 SOONFVTOQRKRALQOFRLPLEETELEKRIIVDDTSTQMSKNMHLIPSTLQOIDEKEE 1380  
DB 1321 SOONFVTOQRKRALQOFRLPLEETELEKRIIVDDTSTQMSKNMHLIPSTLQOIDEKEE 1380  
QY 1381 KGATQSPSLDCLTSHSIPQANSPLPIKVSFSPSIPITLTVLEFODNSSHLPAASY 1440  
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QY 1441 RKKDSVOESSHFLQAGAKNNLSAIIITLMTGDQREVGSLOTSATNSVYTKKENTVLP 1500  
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DB 1501 KPDLPTSGKVELLPKRVHIYOKDLFPTETSNQSPGHLDIYESLLQGTGEGAIKNNEANRP 1560  
QY 1561 GAYPFLRVATESSAKTPSKLLDPLAMDNHYGTQIPKEEKSQEKSPERTAKKKDITLSL 1620  
DB 1561 GAYPFLRVATESSAKTPSKLLDPLAMDNHYGTQIPKEEKSQEKSPERTAKKKDITLSL 1620  
QY 1621 NACESNHAIATINEGONKPEIEVTWAKQRTERLCSQNPVLRKQREITRTTLOSQOEE 1680  
DB 1621 NACESNHAIATINEGONKPEIEVTWAKQRTERLCSQNPVLRKQREITRTTLOSQOEE 1680  
QY 1681 IDDDDTISVEMKKEDPDIDEDENOSPRSQKTRHYFTAAVERLMDYGMSSPHVLRNR 1740  
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QY 1801 PYSFYSLSIYEDDOQAGAEPRKNVKNENKTYFKMKVOHHAAPTRKDEPDCKANAYFSDV 1860  
DB 1801 PYSFYSLSIYEDDOQAGAEPRKNVKNENKTYFKMKVOHHAAPTRKDEPDCKANAYFSDV 1860  
QY 1861 DLEKDVHSGLIGPLVCHNTNLNPAHGRQYVQEFALFETIETDKSWIETENNERNCRA 1920  
DB 1861 DLEKDVHSGLIGPLVCHNTNLNPAHGRQYVQEFALFETIETDKSWIETENNERNCRA 1920

QY 1921 PCNIOMEDPFERENYRFAHNGYIMDTLPGIYNAOQRIKMTLLSMKSNENHSHRPSGH 1980  
DB 1921 PCNIOMEDPFERENYRFAHNGYIMDTLPGIYNAOQRIKMTLLSMKSNENHSHRPSGH 1980  
QY 1981 VFVYRKKEEYKMAIYNLYGVFENVEMLPKAGIMHVECLIGEHHAQMSITLFLVSNKC 2040  
DB 1981 VFVYRKKEEYKMAIYNLYGVFENVEMLPKAGIMHVECLIGEHHAQMSITLFLVSNKC 2040  
QY 2041 QTPLGMASSHIRDFQITASGOYGOMAPKLARLHSGSINASTKEPFSWIVDILAPMTI 2100  
DB 2041 QTPLGMASSHIRDFQITASGOYGOMAPKLARLHSGSINASTKEPFSWIVDILAPMTI 2100  
QY 2101 HGITOGARQKFSILYISOFTIMYSLODKKQYRGNSGTILMVFEGVNDSSGIRKHNFN 2160  
DB 2101 HGITOGARQKFSILYISOFTIMYSLODKKQYRGNSGTILMVFEGVNDSSGIRKHNFN 2160  
QY 2161 PPIIARIYRLPHPHYSIRSTLMLMELMGCDLNSGMPLGMSKASIDAOITASVFTMFA 2220  
DB 2161 PPIIARIYRLPHPHYSIRSTLMLMELMGCDLNSGMPLGMSKASIDAOITASVFTMFA 2220  
QY 2221 TWSPSKARLHLQGRSNAMRPQYNNPKEMVLQVFOKTKRYVTGVTGVSLLTSMYKEFL 2280  
DB 2221 TWSPSKARLHLQGRSNAMRPQYNNPKEMVLQVFOKTKRYVTGVTGVSLLTSMYKEFL 2280  
QY 2281 ISSSQDGHQMTLFPONGKVKYVQGNDSFTPVNSLDPPLTRTYLRIPHQSVHOIALRM 2340  
DB 2281 ISSSQDGHQMTLFPONGKVKYVQGNDSFTPVNSLDPPLTRTYLRIPHQSVHOIALRM 2340  
QY 2341 EYLGEAODLY 2351  
DB 2341 EYLGEAODLY 2351  
  
RESULT 78  
AAW11376  
ID AAW11376 standard; Protein; 2350 AA.  
XX  
AC AAW11376;  
DT 18-NOV-1997 (first entry)  
XX  
DE Active Factor VIII:C analogue delta 335.  
XX  
KW Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;  
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KW plasma protease; thrombin; immunogen; antibody; haemophilia; therapy;  
XX proteolytic cleavage.  
OS Homo sapiens.  
XX Synthetic.  
XX  
FH Key  
FT Peptide  
FT 1..19 Location/Qualifiers  
FT Protein 20..2350 /note= "signal peptide"  
FT 20..2350 /note= "mature Factor VIII:C"  
FT Region 20..1667 /note= "heavy chain fragment"  
FT Modified-site 353..354 /note= "site of 1 residue deletion"  
FT 1668..2349 /note= "light chain fragment"  
FT Domain 760..1667 /note= "B domain"  
XX  
XX W09703195-A1.  
XX 30-JAN-1997.  
XX  
XX 09-JUL-1996; 96MO-US11444.  
XX 11-JUL-1995; 95US-0001025.  
XX

PA (CHIR ) CHIRON CORP.  
XX  
PI Cohen FE, Hung DT, Innis M;  
XX  
DR WPI; 1997-119050/11.  
XX  
PT Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophilias, by improvement of  
PT haemostasis  
XX  
PS  
XX  
PS Claim 18; Page -: 90pp; English.  
XX  
CC AAM1330-M1472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophilias, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
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SQ Sequence 2350 AA;  
Query Match 99.9%; Score 12403.5; DB 18; Length 2350;  
Best Local Similarity 100.0%; Pred. No. 0;  
Matches 2350; Conservative 0; Mismatches 0; Indels 1; Gaps 1;  
QY 1 MOELSTCFELCLRLPCFSATRRRYLGAVELSMDYMOSSDGLPVDARPPRPVPSPEFN 60  
DB 1 MOELSTCFELCLRLPCFSATRRRYLGAVELSMDYMOSSDGLPVDARPPRPVPSPEFN 60  
QY 61 TSVVYKKTLEFEFTDHLFNIAKRPRPMGLGPTIOAEVYDYVTITLKMAHSPSLHAY 120  
DB 61 TSVVYKKTLEFEFTDHLFNIAKRPRPMGLGPTIOAEVYDYVTITLKMAHSPSLHAY 120  
QY 121 GVSYKASBEGAEVDDQTSOREKEDDKVPPGSHYVWQYLKENGPRASDPLCLTYSLSH 180  
DB 121 GVSYKASBEGAEVDDQTSOREKEDDKVPPGSHYVWQYLKENGPRASDPLCLTYSLSH 180  
QY 121 GVSYKASBEGAEVDDQTSOREKEDDKVPPGSHYVWQYLKENGPRASDPLCLTYSLSH 180  
DB 121 GVSYKASBEGAEVDDQTSOREKEDDKVPPGSHYVWQYLKENGPRASDPLCLTYSLSH 180  
QY 181 VDLVNDLNSGLIGALLVCREGSLAKEKTQTLAKFTLLFAVFDGKSMHSETKNSLMODRD 240  
DB 181 VDLVNDLNSGLIGALLVCREGSLAKEKTQTLAKFTLLFAVFDGKSMHSETKNSLMODRD 240  
QY 241 AASARAMPKMTVNGYVNRSLPGLIGCHRKSYVNHVIGMGTPREVSITLBEHTFLVNH 300  
DB 241 AASARAMPKMTVNGYVNRSLPGLIGCHRKSYVNHVIGMGTPREVSITLBEHTFLVNH 300  
QY 241 AASARAMPKMTVNGYVNRSLPGLIGCHRKSYVNHVIGMGTPREVSITLBEHTFLVNH 300  
DB 241 AASARAMPKMTVNGYVNRSLPGLIGCHRKSYVNHVIGMGTPREVSITLBEHTFLVNH 300  
QY 301 ROASSTSPITELTAOGLIMDLGOPLICHTSHSHQHDGMAAYVYKVSCEPEQLMKNE 360  
DB 301 ROASSTSPITELTAOGLIMDLGOPLICHTSHSHQHDGMAAYVYKVSCEPEQLMKNE 360  
QY 301 ROASSTSPITELTAOGLIMDLGOPLICHTSHSHQHDGMAAYVYKVSCEPEQLMKNE 360  
DB 301 ROASSTSPITELTAOGLIMDLGOPLICHTSHSHQHDGMAAYVYKVSCEPEQLMKNE 360  
QY 361 EAEDYDDDLTJSEMDVVRFPDDNSPSFIOIRSVAKKHKPTWVHYIAAEEEDMDYAPLVA 419  
DB 361 EAEDYDDDLTJSEMDVVRFPDDNSPSFIOIRSVAKKHKPTWVHYIAAEEEDMDYAPLVA 419  
QY 421 PDDRSYKSOYLNNGPORIGRKRYKVFMAVYTDDEFKTRREALIQESGILPLLYGEGDTL 480  
DB 421 PDDRSYKSOYLNNGPORIGRKRYKVFMAVYTDDEFKTRREALIQESGILPLLYGEGDTL 480  
QY 421 PDDRSYKSOYLNNGPORIGRKRYKVFMAVYTDDEFKTRREALIQESGILPLLYGEGDTL 480  
DB 421 PDDRSYKSOYLNNGPORIGRKRYKVFMAVYTDDEFKTRREALIQESGILPLLYGEGDTL 480  
QY 481 LIIFFNOASRPYNTYPRGIDVPRPLYSRRLPKGVKHLKDPRIILGRIFFKXKTYVDEGR 540  
DB 481 LIIFFNOASRPYNTYPRGIDVPRPLYSRRLPKGVKHLKDPRIILGRIFFKXKTYVDEGR 540

DB 480 LIIFFNOASRPYNTYPRGIDVPRPLYSRRLPKGVKHLKDPRIILGRIFFKXKTYVDEGR 539  
QY 541 TKSDPCLTRYSSFYNNMERDLASLIGPPLLCYKSSVDQROQIMSKRVILFSEYDE 600  
DB 540 TKSDPCLTRYSSFYNNMERDLASLIGPPLLCYKSSVDQROQIMSKRVILFSEYDE 599  
QY 601 NRSWYLTENIQRFPLNPAGVQLEDEPEFQASNMHSINGVYFSDQLSVCLAEVAYWYILS 660  
DB 600 NRSWYLTENIQRFPLNPAGVQLEDEPEFQASNMHSINGVYFSDQLSVCLAEVAYWYILS 659  
QY 661 IGAOTDFLSVFSGYFHKHKWYEDTLFLPPESGEYFEMSPGLMTLIGCHNSDPNRNG 720  
DB 660 IGAOTDFLSVFSGYFHKHKWYEDTLFLPPESGEYFEMSPGLMTLIGCHNSDPNRNG 719  
QY 721 MTALLKVSQCDKNTGYEDSYEDISAYLLSKNNAIEPNSFQNSRHPSTROKOFNATTT 780  
DB 720 MTALLKVSQCDKNTGYEDSYEDISAYLLSKNNAIEPNSFQNSRHPSTROKOFNATTT 779  
QY 781 PENDIEKTDPMFAHRTPMKIONVSSDLMLLHOSPTPHGLSLDLEAKYEFSDPS 840  
DB 780 PENDIEKTDPMFAHRTPMKIONVSSDLMLLHOSPTPHGLSLDLEAKYEFSDPS 839  
QY 841 PCATDSNNSTSEMTNRRPOLHSGDMFTPPSGIOLAHXIGTTAAATELKKLDFKYSST 900  
DB 840 PCATDSNNSTSEMTNRRPOLHSGDMFTPPSGIOLAHXIGTTAAATELKKLDFKYSST 899  
QY 901 SNNLITSPDNLACGTDTSSLAGPPSPVHYDSQDLTTLFGKSSPLTESGGLSLEE 960  
DB 900 SNNLITSPDNLACGTDTSSLAGPPSPVHYDSQDLTTLFGKSSPLTESGGLSLEE 959  
QY 961 NNDKSLLESGILMOSBSSGKVVSTESGRLFKKRAHGPALLTDNALFVYSISLKTN 1020  
DB 960 NNDKSLLESGILMOSBSSGKVVSTESGRLFKKRAHGPALLTDNALFVYSISLKTN 1019  
QY 1021 KTSNNSATNRKTHIDPSILLIENSVMQNTLSEDPTEFKKVTPLIHDMLDKNAATLRL 1080  
DB 1020 KTSNNSATNRKTHIDPSILLIENSVMQNTLSEDPTEFKKVTPLIHDMLDKNAATLRL 1079  
QY 1081 NMSKRTTSSKNMEOVQKKEGPIPPDONPDSFFKMLFLPESARWIORTHGKNSLNG 1140  
DB 1080 NMSKRTTSSKNMEOVQKKEGPIPPDONPDSFFKMLFLPESARWIORTHGKNSLNG 1139  
QY 1141 QGPSPKOLVSLGPEKSYEGQNTLSEKNVYVVGKEPFDVGLKEWFPSSNNLPLTJMLDN 1200  
DB 1140 QGPSPKOLVSLGPEKSYEGQNTLSEKNVYVVGKEPFDVGLKEWFPSSNNLPLTJMLDN 1199  
QY 1201 LHENTTHOEKKTQOELEKKEKTLIOENVVLOIHTVYGTGKPKNPLFLSTRQVBSYD 1260  
DB 1200 LHENTTHOEKKTQOELEKKEKTLIOENVVLOIHTVYGTGKPKNPLFLSTRQVBSYD 1259  
QY 1261 GAYAVVLQDFRSLNDSTNRTKKNHAFSKKGEENLEGLQNOTKOIVERYACTTRISPNT 1320  
DB 1260 GAYAVVLQDFRSLNDSTNRTKKNHAFSKKGEENLEGLQNOTKOIVERYACTTRISPNT 1319  
QY 1321 SOONFVTOGRKRALQORPLLEBETELERIIIVDDTSTOWSKNNKHLFSTPLQDYNKE 1380  
DB 1320 SOONFVTOGRKRALQORPLLEBETELERIIIVDDTSTOWSKNNKHLFSTPLQDYNKE 1379  
QY 1381 KGAITOSPISDCLTRHSSTPOANRSPPLTAIVSSFSPIRYTLTVLRODMSHLPASV 1440  
DB 1380 KGAITOSPISDCLTRHSSTPOANRSPPLTAIVSSFSPIRYTLTVLRODMSHLPASV 1439  
QY 1441 RAKDSGVOESSHFLQAKKNNLSLAIIITLBMTGQOREVSGLSGATSNSYTKKVENTVLP 1500  
DB 1440 RAKDSGVOESSHFLQAKKNNLSLAIIITLBMTGQOREVSGLSGATSNSYTKKVENTVLP 1499  
QY 1501 KPDLPTKSGKVELLPKNIYIKDLPPTETSGSGHIDLVEGSLQGTGGAIKKNEANRP 1560  
DB 1500 KPDLPTKSGKVELLPKNIYIKDLPPTETSGSGHIDLVEGSLQGTGGAIKKNEANRP 1559  
QY 1561 GVPPLRVATESSAKPPSKLPLDLMDNHVGTQIPKBEKMSOEKSPERTAKKKDITLSL 1620  
DB 1560 GVPPLRVATESSAKPPSKLPLDLMDNHVGTQIPKBEKMSOEKSPERTAKKKDITLSL 1619

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QY 1621 NACSNHAIATAINEGONKPEIEVTWAKOGRTERLCSQNPVLKRHOREITRTTLOSDOE 1680
DB 1620 NACSNHAIATAINEGONKPEIEVTWAKOGRTERLCSQNPVLKRHOREITRTTLOSDOE 1679
QY 1681 IDYDITISVEMKKEDDIYDEDENOSPRSPQKTRHYFAAVERLMDYGMSSPHYLRN 1740
DB 1680 IDYDITISVEMKKEDDIYDEDENOSPRSPQKTRHYFAAVERLMDYGMSSPHYLRN 1739
QY 1741 AOGSSVQFKKVVQFQFTDGSFTQPLKRGELNEHLGLGPYIRAEVDNINWTFRRNAS 1800
DB 1740 AOGSSVQFKKVVQFQFTDGSFTQPLKRGELNEHLGLGPYIRAEVDNINWTFRRNAS 1799
QY 1801 PYSFYSSLISYEDDOGAEPKRNFKVKNETKTYFKKVOHNAPTKDEFDCKAMAYPSDY 1860
DB 1800 PYSFYSSLISYEDDOGAEPKRNFKVKNETKTYFKKVOHNAPTKDEFDCKAMAYPSDY 1859
QY 1861 DLEKDVHSGILGPLVCHTNTLNPAHGRQYVQEFALFTIFDETSMYFTENNERNCRA 1920
DB 1860 DLEKDVHSGILGPLVCHTNTLNPAHGRQYVQEFALFTIFDETSMYFTENNERNCRA 1919
QY 1921 PCNIQMEDPTFKENYFNAINGYIMDTLPGLVAAQDQIRMYTLKSGSNENIHSGH 1980
DB 1920 PCNIQMEDPTFKENYFNAINGYIMDTLPGLVAAQDQIRMYTLKSGSNENIHSGH 1979
QY 1981 VFTYRKKKEEKMALYNLYPGVEFVEMLPKAKIMRVECLIGEHLAGMSTLFLVYSNKC 2040
DB 1980 VFTYRKKKEEKMALYNLYPGVEFVEMLPKAKIMRVECLIGEHLAGMSTLFLVYSNKC 2039
QY 2041 QTPLGMAHGHIRDFOTASGOYGMAPKIAARLHYSGSINANSTKPEPMITVDLAPMII 2100
DB 2040 QTPLGMAHGHIRDFOTASGOYGMAPKIAARLHYSGSINANSTKPEPMITVDLAPMII 2099
QY 2101 HGITQAROKFESSLISQFIIMYSLDGKKQYTRGNSGTLMVFFGVNDSSGIAKHIFN 2160
DB 2100 HGITQAROKFESSLISQFIIMYSLDGKKQYTRGNSGTLMVFFGVNDSSGIAKHIFN 2159
QY 2161 PPIIARIYRLHPHYRISRTLMELMGCDLNSCSPMGESKASIDAQITASSYFTMFA 2220
DB 2160 PPIIARIYRLHPHYRISRTLMELMGCDLNSCSPMGESKASIDAQITASSYFTMFA 2219
QY 2221 TWSPSKARLHLGGRSNAMRPQVNNPKEMLOYDQKTMKTYGTTQGVKSLTSMYVEEF 2280
DB 2220 TWSPSKARLHLGGRSNAMRPQVNNPKEMLOYDQKTMKTYGTTQGVKSLTSMYVEEF 2279
QY 2281 ISSSODGHQWTLFPQNGKVKYQGNQDSFTPVVNSLDPPLTRYLRHHPQSWHQAALRM 2340
DB 2280 ISSSODGHQWTLFPQNGKVKYQGNQDSFTPVVNSLDPPLTRYLRHHPQSWHQAALRM 2339
QY 2341 EYLGCQAQDLY 2351
DB 2340 EYLGCQAQDLY 2350

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## RESULT 79

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AAW11358
ID AAW11358 standard; Protein; 2350 AA.
AC AAW11358;
XX 17-NOV-1997 (first entry)
DE Active Factor VIII:C analogue delta 277.
XX
KW Factor VIII:C analogue; glycoprotein; blood coagulation cascade;
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;
KW proteolytic cleavage.
XX
OS Homo sapiens.
OS Synthetic.
XX
FH Key Location/Qualifiers

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FT Peptide 1..19
FT /note= "Signal peptide"
FT Protein 20..2350
FT /note= "mature Factor VIII:C"
FT Region 20..1667
FT /note= "heavy chain fragment"
FT Modified-site 295..296
FT /note= "site of 1 residue deletion"
FT Region 1668..2349
FT /note= "light chain fragment"
FT Domain 760..1667
FT /note= "B domain"
XX
XX WO9703195-A1.
XX
XX 30-JAN-1997.
XX
XX 09-JUL-1996; 96MO-US11444.
XX
XX 11-JUL-1995; 95US-0001025.
XX
XX (CHIR ) CHIRON CORP.
XX
XX Cohen FE, Hung DT, Innis M;
XX
XX MPI: 1997-119050/11.
XX
XX Factor VIII:C analog modified adjacent to a non-activating Arg
XX residue - used in the treatment of haemophilia, by improvement of
XX haemostasis
XX
XX Claim 14; Page -: 90pp; English.
XX
XX AAW11330-W11472 represent active Factor VIII:C analogues of the
XX invention. These sequences were created by mutating the wild type Factor
XX VIII:C coding sequence (see AAT51357) using mutagenic primers. The
XX analogues comprise a native Factor VIII:C polypeptide modified at a site
XX adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
XX dipeptide is created. Factor VIII:C is a large glycoprotein that
XX participates in the blood coagulation cascade that ultimately converts
XX soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
XX deficiency in Factor VIII:C is responsible for haemophilia A, which is an
XX X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
XX activated by plasma proteases, such as thrombin. During activation the
XX mature polypeptide is cleaved to generate heavy and light chain fragments
XX that are further cleaved. Complexes of two or more of the analogues,
XX nucleic acids and vectors encoding them may be used alone or in
XX conjunction with each other, for the prevention or treatment of active
XX Factor VIII:C deficiency in a mammal. The analogues may be used as
XX immunogens to raise antibodies, and in the treatment of haemophilias, by
XX improvement of haemostasis. The analogues are resistant to proteolytic
XX cleavage and display increased plasma half-life. They may be administered
XX at lower dosages and by different modes of administration.
XX
XX Sequence 2350 AA.
XX
XX Query Match 99.98; Score 12403.5; DB 18; Length 2350;
XX Best local Similarity 100.0%; Pred. No. 0;
XX Matches 2350; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

```

181 VDLVKDLSGLIGALLVCRESSLAKEKTOQLHFKFILLPAVFDEGKSMHSETKNSLMDRRD 240  
QY 241 AASARAPKMTYNGVYNSLPGILGHRKSVWHTYIGMCTTPEVHSIFELGHTFLVRNH 300  
Db 241 AASARAPKMTYNGVYNSLPGILGHRKSVWHTYIGMCTTPEVHSIFELGHTFLVRNH 299  
QY 301 ROASDBASPTITFLTAOTJLMDLGOFLFCHLSSHOHDMGEMAVYKVDSCPEEPOLRMKNNE 360  
Db 300 ROASLEISPTITFLTAOTJLMDLGOFLFCHLSSHOHDMGEMAVYKVDSCPEEPOLRMKNNE 359  
QY 361 EAEDYDDDLTDSMDVYRFPDDNNSPFIQIRSAKKHPTWHTYIAAEEEDMDVAPVYLA 420  
Db 360 EAEDYDDDLTDSMDVYRFPDDNNSPFIQIRSAKKHPTWHTYIAAEEEDMDVAPVYLA 419  
QY 421 PDDRSYKSOYLANNGPORIGRKYKKVRFMAATYDEFTKREAIQHSGLIGPLLYGEVCDTL 480  
Db 420 PDDRSYKSOYLANNGPORIGRKYKKVRFMAATYDEFTKREAIQHSGLIGPLLYGEVCDTL 479  
QY 481 LIFRNOASRPYNIYPHGITDVRPLYSRHLPGVKHLDKDFLLPGEIFRKYKWTYVEDGP 540  
Db 480 LIFRNOASRPYNIYPHGITDVRPLYSRHLPGVKHLDKDFLLPGEIFRKYKWTYVEDGP 539  
QY 541 TKSDPCLTRVYSSPFNMERDLASGLIGPLLYCKESVODRGNOIMSDKRWVILFVSFDE 600  
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QY 601 NRSWYLTENIORFLPNPAGVLEDEFOASNIMHSINGVYFDSLOLSVCLHEVAYWYILS 660  
Db 600 NRSWYLTENIORFLPNPAGVLEDEFOASNIMHSINGVYFDSLOLSVCLHEVAYWYILS 659  
QY 661 IGAOTDFLSVFSFGYEFKHKMYEEDTLTFPFSSEYFMSMEMEPGLMILGCHNSDFNRG 720  
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QY 721 MTALLKXSCDKMTGYEDSYEDISATLLSKNNAIPRPSFSONSRHSTOKOPNATTI 780  
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QY 781 PENDIKXTDPMFAHRTPMKIONVSSDLMMLRKOSFPFGHLSLSDLOBAKYETTFSDPS 840  
Db 780 PENDIKXTDPMFAHRTPMKIONVSSDLMMLRKOSFPFGHLSLSDLOBAKYETTFSDPS 839  
QY 841 PGALDSNNLSSEMTHERPOLHHSGDMVFTPESSGLOLRNKGJTTAATELKKDFKXVSST 900  
Db 840 PGALDSNNLSSEMTHERPOLHHSGDMVFTPESSGLOLRNKGJTTAATELKKDFKXVSST 899  
QY 901 SNMLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQDLDTTLFGKSSPLTESGGLSSEE 960  
Db 900 SNMLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQDLDTTLFGKSSPLTESGGLSSEE 959  
QY 961 NNDKSLLESGLMNSOESSWGKNVSTESGRLLFKGRAGPALJTKNALFKVYSISLTKTN 1020  
Db 960 NNDKSLLESGLMNSOESSWGKNVSTESGRLLFKGRAGPALJTKNALFKVYSISLTKTN 1019  
QY 1021 KTSNNSATNRKTHIDPSSLIENSFVYQNTLESDTEFFKVPPLHIDRLMDKNAATLRL 1080  
Db 1020 KTSNNSATNRKTHIDPSSLIENSFVYQNTLESDTEFFKVPPLHIDRLMDKNAATLRL 1079  
QY 1081 NMSKTKTSSKNMMEYQOKKEGPIPPDAQNPDMSFFKMLFLPESARMIORHGNKNSLNG 1140  
Db 1080 NMSKTKTSSKNMMEYQOKKEGPIPPDAQNPDMSFFKMLFLPESARMIORHGNKNSLNG 1139  
QY 1141 QGPPSKOLVSLGPEKSEVQONFLSEKKNVYVVGKEEFTKVDGLKEWFPSSRNLEJTJLND 1200  
Db 1140 QGPPSKOLVSLGPEKSEVQONFLSEKKNVYVVGKEEFTKVDGLKEWFPSSRNLEJTJLND 1199  
QY 1201 LHENNTNHOEKKIOEELKEKTLIOENVLPQIHVTYGTKNPKNLFLLSTRONVBSYD 1260  
Db 1200 LHENNTNHOEKKIOEELKEKTLIOENVLPQIHVTYGTKNPKNLFLLSTRONVBSYD 1259  
QY 1261 GAYAPVLODFRSLNDSTNRKKTAFHFSKKEEENLEGLGNQTKOIVEKYACTTRISPNT 1320  
Db 1261 GAYAPVLODFRSLNDSTNRKKTAFHFSKKEEENLEGLGNQTKOIVEKYACTTRISPNT 1320

Db 1260 GAYAPVLODFRSLNDSTNRKKTAFHFSKKEEENLEGLGNQTKOIVEKYACTTRISPNT 1319  
QY 1321 SOONPTORSKRALKOFRLPEETLEKRIIYVDDTSTONSKMMKHLTFPSTLTOIDYNEKE 1380  
Db 1320 SOONPTORSKRALKOFRLPEETLEKRIIYVDDTSTONSKMMKHLTFPSTLTOIDYNEKE 1379  
QY 1381 KGAITOSPESDCLTRSHSIPQANRSPPLIAKVSSPSPIRIYLVLPQDNSSHLPAAST 1440  
Db 1380 KGAITOSPESDCLTRSHSIPQANRSPPLIAKVSSPSPIRIYLVLPQDNSSHLPAAST 1439  
QY 1441 RKDSGOVESHPLQAGAKNNLSTLILFLEMTGDPORVSGLSGTSATNSVTYKKVENTVLP 1500  
Db 1440 RKDSGOVESHPLQAGAKNNLSTLILFLEMTGDPORVSGLSGTSATNSVTYKKVENTVLP 1499  
QY 1501 KPDLPTSGVELLPVYHLYQDLFPTTSGNSGHLDLVESSLQGTREGALIKNNEANRP 1560  
Db 1500 KPDLPTSGVELLPVYHLYQDLFPTTSGNSGHLDLVESSLQGTREGALIKNNEANRP 1559  
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Db 1560 GKVPFLRVATESAKTPSKLIDLPLAMDNHYGTQIPKEEMKSOEKSPEKTAARKKDTILSL 1619  
QY 1621 NACSNHAIATAINBGNKPEIEVTWAKOGPTEKSONPPVLKRHOEITRTTLOSOOE 1680  
Db 1620 NACSNHAIATAINBGNKPEIEVTWAKOGPTEKSONPPVLKRHOEITRTTLOSOOE 1679  
QY 1681 IDYDDTISVEKKEDFDIYDEBENOSPPSFQKTRHFTJANVERLMDYGNSSPHVLRNR 1740  
Db 1680 IDYDDTISVEKKEDFDIYDEBENOSPPSFQKTRHFTJANVERLMDYGNSSPHVLRNR 1739  
QY 1741 AOSGSVPOFKKVVFOEFTDGSFTOPLYGELNENHILGLPYIRAEVEDNIWVTRNOASR 1800  
Db 1740 AOSGSVPOFKKVVFOEFTDGSFTOPLYGELNENHILGLPYIRAEVEDNIWVTRNOASR 1799  
QY 1801 PYSFSSLSIYEEEDOGAEPKRNKVNKNEKTYFKMVVOHMAPTKDEPDCKANAYESDV 1860  
Db 1800 PYSFSSLSIYEEEDOGAEPKRNKVNKNEKTYFKMVVOHMAPTKDEPDCKANAYESDV 1859  
QY 1861 DLEKDVHSGILGPLLCHTNTLNPAHGNQVTVDEFALFTTIEDETKSWYFTBNERNCRA 1920  
Db 1860 DLEKDVHSGILGPLLCHTNTLNPAHGNQVTVDEFALFTTIEDETKSWYFTBNERNCRA 1919  
QY 1921 PCNIQMEDPTFEKENVFPAHNGYINDTLPGJLVMAQDORIRWYLLSGNSMENHSHIRSGH 1980  
Db 1920 PCNIQMEDPTFEKENVFPAHNGYINDTLPGJLVMAQDORIRWYLLSGNSMENHSHIRSGH 1979  
QY 1981 VFTYPAKKEEYKMAIYLYPGVEFTEVEMLPKAGIMRWECCLIGBHLHAGSTLFLVYSNKC 2040  
Db 1980 VFTYPAKKEEYKMAIYLYPGVEFTEVEMLPKAGIMRWECCLIGBHLHAGSTLFLVYSNKC 2039  
QY 2041 QTPILGMAHGRDFOJTASGOYQONAPKRLARLHSGSINAMSTKEPFSNIVYDLAPMII 2100  
Db 2040 QTPILGMAHGRDFOJTASGOYQONAPKRLARLHSGSINAMSTKEPFSNIVYDLAPMII 2099  
QY 2101 HGIKTOGAROKFESSLYISOFITIMYSLDCKKQYTRGSTGTLWAFVGVNDSSGIKHNIFN 2160  
Db 2100 HGIKTOGAROKFESSLYISOFITIMYSLDCKKQYTRGSTGTLWAFVGVNDSSGIKHNIFN 2159  
QY 2161 PPTIARTIRLAPTHYSIRSLTLMELMAGCDLNSCMPILGMSKASISAOQTASSTFTNMPA 2220  
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QY 2221 TWPSPKARLHLOGRSNANRPVNNKPEMLQYDFOKTKKVTGYTTOGVSKSLTSMYKVEFL 2280  
Db 2220 TWPSPKARLHLOGRSNANRPVNNKPEMLQYDFOKTKKVTGYTTOGVSKSLTSMYKVEFL 2279  
QY 2281 ISSSODGHQWTLFPONGKAYKVOGNODSFTFVNVSLDPLLPRTYLRHHPQSVHIOILRM 2340  
Db 2280 ISSSODGHQWTLFPONGKAYKVOGNODSFTFVNVSLDPLLPRTYLRHHPQSVHIOILRM 2339  
QY 2341 EYLGCEADOLY 2351  
Db 2340 EYLGCEADOLY 2350

RESULT 80  
AAW11359  
ID AAW11359 standard; Protein; 2350 AA.  
XX  
AC AAW11359;  
XX  
XX  
DT 17-NOV-1997 (first entry)  
XX  
DE Active Factor VIII:C analogue delta 278.  
XX  
KM Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;  
KM fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KM plasma protease; thrombin; immunogen; antibody; haemophilia; therapy;  
KM proteolytic cleavage.  
XX  
OS Homo sapiens.  
OS Synthetic.  
XX  
FH Key Location/Qualifiers  
FT Peptide 1..19  
FT /note= "signal peptide"  
FT Protein 20..2350  
FT /note= "mature Factor VIII:C"  
FT Region 20..1667  
FT /note= "heavy chain fragment"  
FT Modified-site 296..297  
FT /note= "site of 1 residue deletion"  
FT Region 1668..2349  
FT /note= "light chain fragment"  
FT Domain 760..1667  
FT /note= "B domain"  
XX  
PN WO9703195-A1.  
XX  
PD 30-JAN-1997.  
XX  
PF 09-JUL-1996; 96MO-US1444.  
XX  
PR 11-JUL-1995; 95US-0001025.  
XX  
PA (CHTR ) CHIRON CORP.  
XX  
PI Cohen FE, Hung DT, Innis M;  
XX  
DR WPI: 1997-119050/11.  
XX  
PT Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophiliacs, by improvement of  
PT haemostasis  
XX  
PS Claim 14; Page -: 90pp; English.  
XX  
CC AAW11330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophiliacs, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered

CC at lower dosages and by different modes of administration.

XX Sequence 2350 AA:

Query Match 99.9%; Score 12403.5; DB 18; Length 2350;

Best local Similarity 100.0%; Pred. No. 0;  
Matches 2350; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

QY 1 MQELSTCFPLCLRCPSATRRYYLAVALSDMDYQSDGLPVDAPFRPRPKSPFN 60  
DB 1 MQELSTCFPLCLRCPSATRRYYLAVALSDMDYQSDGLPVDAPFRPRPKSPFN 60  
QY 61 TSYYKKTLFVEFTDHLFNIAKPRPMMGLGPTIOAEYDVTVITLKNMASHVSLAAV 120  
DB 61 TSYYKKTLFVEFTDHLFNIAKPRPMMGLGPTIOAEYDVTVITLKNMASHVSLAAV 120  
QY 121 GVSYWKASGAEYDQTSQREKEDKVPFGSHTYYWQVLKENGPMASDPLCLTYSTLSH 180  
DB 121 GVSYWKASGAEYDQTSQREKEDKVPFGSHTYYWQVLKENGPMASDPLCLTYSTLSH 180  
QY 181 VDLVKDLSGLIGALLVCRESGLAKETQTLKFTLLFVPEBGSMSHSETKNSLMQDD 240  
DB 181 VDLVKDLSGLIGALLVCRESGLAKETQTLKFTLLFVPEBGSMSHSETKNSLMQDD 240  
QY 241 AASARAMPKMHVNGVYKNSLPGILGCHRSYVWVHVGMTTPEVHSIFLEGHTFLRNH 300  
DB 241 AASARAMPKMHVNGVYKNSLPGILGCHRSYVWVHVGMTTPEVHSIFLEGHTFLRNH 300  
QY 301 ROSLEISPTFTTAAELTMDLGOFTLLFCHSSHODGMEAVVKKDSCPEEPOLRMKNNE 360  
DB 301 ROSLEISPTFTTAAELTMDLGOFTLLFCHSSHODGMEAVVKKDSCPEEPOLRMKNNE 360  
QY 361 EADYDDDLTDSMDVYRFDNDSPTQIRSYAKKHPRKTVWVHTAAEEDMDYAPLVTA 420  
DB 361 EADYDDDLTDSMDVYRFDNDSPTQIRSYAKKHPRKTVWVHTAAEEDMDYAPLVTA 420  
QY 421 PDDRSYSQYLLNNGPQIRGRYKKKRRMATDTEFTFTRAIOHESGILGPLYGEVDTL 480  
DB 421 PDDRSYSQYLLNNGPQIRGRYKKKRRMATDTEFTFTRAIOHESGILGPLYGEVDTL 480  
QY 481 LIIFKNASRPVNTYHGTVDYRPLYSRRLPKVKYLKKEFTLLBEIFKRYWVYEDDP 540  
DB 481 LIIFKNASRPVNTYHGTVDYRPLYSRRLPKVKYLKKEFTLLBEIFKRYWVYEDDP 540  
QY 541 TKSDPRCLTRYSSFFVNMERDLASGLIGPLLICYKESVDORGNQIMSDKRVILFSYDE 600  
DB 541 TKSDPRCLTRYSSFFVNMERDLASGLIGPLLICYKESVDORGNQIMSDKRVILFSYDE 600  
QY 601 NRSWYLTENTIORFLPPAGVQLEDEPFOASINHSINGVFPISQLSVCLHEVAWYVILS 660  
DB 601 NRSWYLTENTIORFLPPAGVQLEDEPFOASINHSINGVFPISQLSVCLHEVAWYVILS 660  
QY 661 IGAOTDPLSVFSGYTFKHKMYEDTLTLRPFSGEYFVPMENPCLMTLGHNSDRRNG 720  
DB 661 IGAOTDPLSVFSGYTFKHKMYEDTLTLRPFSGEYFVPMENPCLMTLGHNSDRRNG 720  
QY 721 MTALLKVSQCKNKTGDEYEDSAYLLSKNNALTEPRFSQNSRHPSTROKOFANATTI 780  
DB 721 MTALLKVSQCKNKTGDEYEDSAYLLSKNNALTEPRFSQNSRHPSTROKOFANATTI 780  
QY 781 PENIIEKTDWFAHRRPMPKIONVSSDMLMLROSPRHGSLSDLOEAKYETFSDDPS 840  
DB 781 PENIIEKTDWFAHRRPMPKIONVSSDMLMLROSPRHGSLSDLOEAKYETFSDDPS 840  
QY 841 PGALDSNNLSLEMTNHRPOLNHSQDWVTPESGLDRLNEKIGTTAATELKKLDFVYSST 900  
DB 841 PGALDSNNLSLEMTNHRPOLNHSQDWVTPESGLDRLNEKIGTTAATELKKLDFVYSST 900  
QY 901 SNNIISTIPSDNLAAGTNTSSILPRPMPVNYHYSQDITLRFKKSSTPTESSGRLSLEE 960  
DB 901 SNNIISTIPSDNLAAGTNTSSILPRPMPVNYHYSQDITLRFKKSSTPTESSGRLSLEE 960  
QY 961 NNSKLLIESGLMNSQESWGMKNVSTESGRLFGKRAHGRPALITKDNALFKVYSISLTKTN 1020



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Db      960  NNDSTLESGLMNSQESMCKNVSSGESRLFKGRAGPALTLTKNALFKSISILKTN 1019
Qy      1021  KTSNNSATNRKTHIDGSLIENSPTWONLLESPTPEKVTPLIDHRLMKKATLRL 1080
Db      1020  KTSNNSATNRKTHIDGSLIENSPTWONLLESPTPEKVTPLIDHRLMKKATLRL 1079
Qy      1081  NMSNKTTSKKNMEMVOOKKEGPIPPDAQNPDMSFKMLFLPSASAWIORTGKNSLNSG 1140
Db      1080  NMSNKTTSKKNMEMVOOKKEGPIPPDAQNPDMSFKMLFLPSASAWIORTGKNSLNSG 1139
Qy      1141  QGSPKQQLVSLGPEKSEYEGONFLSEKNKVVYKQGEFTKDVGLKEMVFPSSRLPLTNND 1280
Db      1140  QGSPKQQLVSLGPEKSEYEGONFLSEKNKVVYKQGEFTKDVGLKEMVFPSSRLPLTNND 1199
Qy      1201  LHENNTHOEKKIOEELIEKKEKTLIGENVVLPQIHVTGCTKNPKNFLLSTQONVEGSD 1260
Db      1200  LHENNTHOEKKIOEELIEKKEKTLIGENVVLPQIHVTGCTKNPKNFLLSTQONVEGSD 1259
Qy      1261  GAYAVVLQDFRSLDSTNRTKHTAHFSKGBEENLEGLNQTKQIYEKYACTRISPT 1320
Db      1260  GAYAVVLQDFRSLDSTNRTKHTAHFSKGBEENLEGLNQTKQIYEKYACTRISPT 1319
Qy      1321  SOONFVTOGRKRALKORPLFEETLEKRIIVDOSTOMSKNKHLPSTLTQIDYNEKE 1380
Db      1320  SOONFVTOGRKRALKORPLFEETLEKRIIVDOSTOMSKNKHLPSTLTQIDYNEKE 1379
Qy      1381  KGAITQSPSLDCLTRSHSIPQANRSPPLAKVSSPSIRPIYLRVLPQDNSSHLPAASY 1440
Db      1380  KGAITQSPSLDCLTRSHSIPQANRSPPLAKVSSPSIRPIYLRVLPQDNSSHLPAASY 1439
Qy      1441  RKDSGVOESSHFLQGAKKNNLSLALTLLEMTGDOREVSGISAVNSYTKYKVENYVLP 1500
Db      1440  RKDSGVOESSHFLQGAKKNNLSLALTLLEMTGDOREVSGISAVNSYTKYKVENYVLP 1499
Qy      1501  KPDLPTSGKVELLPKHIIYQKDLPTETSNCSRGHDLVBGSLQGTGALKMEANRP 1560
Db      1500  KPDLPTSGKVELLPKHIIYQKDLPTETSNCSRGHDLVBGSLQGTGALKMEANRP 1559
Qy      1561  GAYPFLVATBSSAKTSTKLLDPLAMDNHYGTQIPREBMSQKSEPKTAFKKDTIISL 1620
Db      1560  GAYPFLVATBSSAKTSTKLLDPLAMDNHYGTQIPREBMSQKSEPKTAFKKDTIISL 1619
Qy      1621  NACESNHAIAINEGOKPEIEVYMAKOGRTERLCSQNPVLARKHOREITRTTLOSDEE 1680
Db      1620  NACESNHAIAINEGOKPEIEVYMAKOGRTERLCSQNPVLARKHOREITRTTLOSDEE 1679
Qy      1681  IDYDPTISVEKKKEDPIYDEENOSPRSFOKTRHYETIAVERLMDYGSSSPHVLNKR 1740
Db      1680  IDYDPTISVEKKKEDPIYDEENOSPRSFOKTRHYETIAVERLMDYGSSSPHVLNKR 1739
Qy      1741  AOSGSVPQFKVVFQETDGSFTQPLYRGELNEHLGLGPYIRAEVEDNINVTFRNOASR 1800
Db      1740  AOSGSVPQFKVVFQETDGSFTQPLYRGELNEHLGLGPYIRAEVEDNINVTFRNOASR 1799
Qy      1801  PYSFYSLSIYEEDORQGAERKNPFYKMETKYFMKVQOHMAPTKDEPDCAKAMVFFDV 1860
Db      1800  PYSFYSLSIYEEDORQGAERKNPFYKMETKYFMKVQOHMAPTKDEPDCAKAMVFFDV 1859
Qy      1861  DLEKDVHSLGLLPLVCHTNTLPAHGRQVYQVDEALFPTIPDETYSWFTNMERNCR 1920
Db      1860  DLEKDVHSLGLLPLVCHTNTLPAHGRQVYQVDEALFPTIPDETYSWFTNMERNCR 1919
Qy      1921  PCNIQMEDPTREKNTREHAIINGYIMDTLPGLVAMODORIMYILSGSNENHSHIFEGH 1980
Db      1920  PCNIQMEDPTREKNTREHAIINGYIMDTLPGLVAMODORIMYILSGSNENHSHIFEGH 1979
Qy      1981  VFTVARKKEEYKALYNLYPGVFETVEMLPKSKAGIMRVECLIGHLIAGNSTFLVYSKC 2040
Db      1980  VFTVARKKEEYKALYNLYPGVFETVEMLPKSKAGIMRVECLIGHLIAGNSTFLVYSKC 2039
Qy      2041  QTPILGMSGHIRDFOITASQGYQMAPKLARLHYSGSINAMSTKEPFSWIKVDLLAPMI 2100

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Db      2040  QTPILGMSGHIRDFOITASQGYQMAPKLARLHYSGSINAMSTKEPFSWIKVDLLAPMI 2099
Qy      2101  HGKTQGAROKFSSLYTSOFTIMYSLDGKKWQTRKGNSTGLWVFFGNDSGJAHNIFN 2160
Db      2100  HGKTQGAROKFSSLYTSOFTIMYSLDGKKWQTRKGNSTGLWVFFGNDSGJAHNIFN 2159
Qy      2161  PPIIARYIRLHPHYSTRSTLRNMLGCDLNSCSMPGLMESKASIDAOITASSYPTNMA 2220
Db      2160  PPIIARYIRLHPHYSTRSTLRNMLGCDLNSCSMPGLMESKASIDAOITASSYPTNMA 2219
Qy      2221  TWSPSKARLHLOGRNMARPOVNNPEKMLQVDPOKTKVYGTTOGKSLTSMYKREFL 2280
Db      2220  TWSPSKARLHLOGRNMARPOVNNPEKMLQVDPOKTKVYGTTOGKSLTSMYKREFL 2279
Qy      2281  ISSODGHQWTLFPOKRVKVFQGNDSFTPYVNSLDPPLLTRYLRIHQSWHQAIALRM 2340
Db      2280  ISSODGHQWTLFPOKRVKVFQGNDSFTPYVNSLDPPLLTRYLRIHQSWHQAIALRM 2339
Qy      2341  EVLGEADOLY 2351
Db      2340  EVLGEADOLY 2350

RESULT 81
AAW10591
ID   AAW10591 standard; protein; 2351 AA.
XX
XX   AAW10591:
XX
XX   03-DEC-1997 (first entry)
XX
XX   Factor VIII:C (Phe652His).
DE
XX
XX   Factor VIII:C: F8C; Factor V A: Factor V C; domain; F8C deficiency;
KW   haemophilia A; blood clotting disorder; immunogen; antibody.
XX
XX   Homo sapiens.
OS
XX
XX   Key
FH   Peptide
FT   /note= "Signal peptide"
FT   /note= "20..2351"
FT   Protein
FT   /note= "Mature factor VIII:C"
FT   Misc-difference 671
FT   /label= Phe652His
XX
XX   MO9703191-A1.
XX
XX   30-JAN-1997.
XX
XX   28-JUN-1996; 96MO-US11013.
XX
XX   11-JUL-1995; 95US-0001030.
XX
XX   (CHIR ) CHIRON CORP.
XX
XX   PA
XX   PI
XX   Hung DT:
XX
XX   WPI: 1997-119047/11.
XX
XX   Claim 6: Page -: 45pp; English.
XX
XX   The sequences given in M10590-92 represent active Factor VIII:C (F8C)
XX   polypeptide analogues. These analogues comprises a native F8C
XX   C domain and/or subdomain. The F8C polypeptide analogues, alone or in
XX   combination, can be used for the prevention or treatment of an active
XX   F8C deficiency, i.e. haemophilia A and other blood clotting disorders.
XX   The analogues can also be used as an immunogen for antibody production.
XX   The analogues can have an increased plasma half-life, or specific

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CC activity. This sequence is not given in the specification and is  
CC based on the sequence derived from Genbank ref. K01740.

XX Sequence 2351 AA:

Query Match 99.9%; Score 12402; DB 18; Length 2351;  
Best local similarity 99.9%; Pred. No. 0;  
Matches 2348; Conservative 2; Mismatches 1; Indels 0; Gaps 0;

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QY 1 MOIELSTCFCLLRCSATRRYYLGAVELSMYQMSDGLPDPARPPRVKSPEN 60
DB 1 MOIELSTCFCLLRCSATRRYYLGAVELSMYQMSDGLPDPARPPRVKSPEN 60
QY 61 TSVYKKTLFEVETDILFNIAKPRPMGILLGPTIQAEVYDVVTLLKNMASHPSLHAV 120
DB 61 TSVYKKTLFEVETDILFNIAKPRPMGILLGPTIQAEVYDVVTLLKNMASHPSLHAV 120
QY 121 GYSYWKASGEAEYDDOTSOREKEDKVPGGSHTYVMQYLKENGPMASDPLCLTYSLSH 180
DB 121 GYSYWKASGEAEYDDOTSOREKEDKVPGGSHTYVMQYLKENGPMASDPLCLTYSLSH 180
QY 122 CYSYWKASGEAEYDDOTSOREKEDKVPGGSHTYVMQYLKENGPMASDPLCLTYSLSH 180
DB 122 CYSYWKASGEAEYDDOTSOREKEDKVPGGSHTYVMQYLKENGPMASDPLCLTYSLSH 180
QY 181 VDLVKDLNSGLIGALLVCRESSLAKETQTLHKFILLFAVFDGSKMHSKSLMODRD 240
DB 181 VDLVKDLNSGLIGALLVCRESSLAKETQTLHKFILLFAVFDGSKMHSKSLMODRD 240
QY 181 VDLVKDLNSGLIGALLVCRESSLAKETQTLHKFILLFAVFDGSKMHSKSLMODRD 240
DB 181 VDLVKDLNSGLIGALLVCRESSLAKETQTLHKFILLFAVFDGSKMHSKSLMODRD 240
QY 241 AASARAMPKMHVNGVYVNSRLPGLIGCHRSKVYWHVIGMGTPEVHSIFLEGHTFLVRNH 300
DB 241 AASARAMPKMHVNGVYVNSRLPGLIGCHRSKVYWHVIGMGTPEVHSIFLEGHTFLVRNH 300
QY 301 ROASLEISPTFLTAOTLMDIGOFILCHSHSHOHGMAYKYKDSPEPQOLRMKNE 360
DB 301 ROASLEISPTFLTAOTLMDIGOFILCHSHSHOHGMAYKYKDSPEPQOLRMKNE 360
QY 301 ROASLEISPTFLTAOTLMDIGOFILCHSHSHOHGMAYKYKDSPEPQOLRMKNE 360
DB 301 ROASLEISPTFLTAOTLMDIGOFILCHSHSHOHGMAYKYKDSPEPQOLRMKNE 360
QY 361 EAEDYDDDLTDSMDVYRFDDDNSSPSIQIRSVAKKHPTKWTWYIAEBEDMDAPLVLA 420
DB 361 EAEDYDDDLTDSMDVYRFDDDNSSPSIQIRSVAKKHPTKWTWYIAEBEDMDAPLVLA 420
QY 361 EAEDYDDDLTDSMDVYRFDDDNSSPSIQIRSVAKKHPTKWTWYIAEBEDMDAPLVLA 420
DB 361 EAEDYDDDLTDSMDVYRFDDDNSSPSIQIRSVAKKHPTKWTWYIAEBEDMDAPLVLA 420
QY 421 PDDRSYKSOYLNNGPORIGRKYKKRFMAVYDEFFKTRREALIQHESGILGPLYEGVDTL 480
DB 421 PDDRSYKSOYLNNGPORIGRKYKKRFMAVYDEFFKTRREALIQHESGILGPLYEGVDTL 480
QY 481 LIIFPNQASRPYNIYHGITDVRPLYSRPLKYGKHLKDPILLPGIRKYKWTYVADGP 540
DB 481 LIIFPNQASRPYNIYHGITDVRPLYSRPLKYGKHLKDPILLPGIRKYKWTYVADGP 540
QY 541 TKSDEPCLTRYYSFVNMERDLASGLIGPLLIYKESVDORGNOIMSDKRVYLLFSVDE 600
DB 541 TKSDEPCLTRYYSFVNMERDLASGLIGPLLIYKESVDORGNOIMSDKRVYLLFSVDE 600
QY 601 NRSWYLTENIQRFLLPMPAGVQLEDEPEFQASIMHSINGYFDSIQLSVCLREVAVWYILS 660
DB 601 NRSWYLTENIQRFLLPMPAGVQLEDEPEFQASIMHSINGYFDSIQLSVCLREVAVWYILS 660
QY 661 IGAOTDPLSVFSGYFHKHMYEDTLTPFPSESEYFVSKMERGMILGCHNSDFNRNG 720
DB 661 IGAOTDPLSVFSGYFHKHMYEDTLTPFPSESEYFVSKMERGMILGCHNSDFNRNG 720
QY 721 MTALLKVSQCDKNTGDIYEDSYEDISAVLLSKNNALIPRSFSONSHSTROKOFNATTT 780
DB 721 MTALLKVSQCDKNTGDIYEDSYEDISAVLLSKNNALIPRSFSONSHSTROKOFNATTT 780
QY 781 PENDEIKTDPMFAHRTPMKIQNVSSDMLMLLQSPTPHIGLSLQDEAKYEFFSDDPS 840
DB 781 PENDEIKTDPMFAHRTPMKIQNVSSDMLMLLQSPTPHIGLSLQDEAKYEFFSDDPS 840
QY 841 PGALDSNNSLSEMTYHRRFQOLHHSQDMVTTPSSGQLALNKAGTTAATLKKLDFKYST 900
DB 841 PGALDSNNSLSEMTYHRRFQOLHHSQDMVTTPSSGQLALNKAGTTAATLKKLDFKYST 900
QY 901 SNNLISITPSDNLAAAGTDMTSSLAGPSMPVYDSQDLDTTLFGKSSPLTESGGLSSEE 960
DB 901 SNNLISITPSDNLAAAGTDMTSSLAGPSMPVYDSQDLDTTLFGKSSPLTESGGLSSEE 960
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QY 961 NNDKSLLESGIMNSQESSGNKVNSTSEGRLEFGKRAHGPALLITDONALEVYSILKTN 1020
DB 961 NNDKSLLESGIMNSQESSGNKVNSTSEGRLEFGKRAHGPALLITDONALEVYSILKTN 1020
QY 1021 KTSNNSATNKRTHIDPSPILLIENSFWONILSDTEFFKVTPLIHDHMLMDKNATLRL 1080
DB 1021 KTSNNSATNKRTHIDPSPILLIENSFWONILSDTEFFKVTPLIHDHMLMDKNATLRL 1080
QY 1081 NMSNKTSSKNMNMVQOKKEGPIPPAONPDMSPFKMLFLPESARVQRTGKNSLNSG 1140
DB 1081 NMSNKTSSKNMNMVQOKKEGPIPPAONPDMSPFKMLFLPESARVQRTGKNSLNSG 1140
QY 1141 QGSPKOLVSLGPEKSEGOFLSEKKNVVGGEFTKDVGLAKEVFPSSNULFLINLDN 1200
DB 1141 QGSPKOLVSLGPEKSEGOFLSEKKNVVGGEFTKDVGLAKEVFPSSNULFLINLDN 1200
QY 1201 LHENNTNOKKIQEIEEKKETLQIENVVLPOIHTYGTNFKPMKMLFLSTROMVEGYD 1260
DB 1201 LHENNTNOKKIQEIEEKKETLQIENVVLPOIHTYGTNFKPMKMLFLSTROMVEGYD 1260
QY 1261 GAYAPVLQDFRSLNDSTNRTKHTAHRSKGEENLEGLGNQTKOIVKTYACTTRISPNT 1320
DB 1261 GAYAPVLQDFRSLNDSTNRTKHTAHRSKGEENLEGLGNQTKOIVKTYACTTRISPNT 1320
QY 1321 SQONFVTVQSRKRALKOFRLPLEETELEKRIIVDSTQMSKMMKHLFPSLTQIDYNEKE 1380
DB 1321 SQONFVTVQSRKRALKOFRLPLEETELEKRIIVDSTQMSKMMKHLFPSLTQIDYNEKE 1380
QY 1381 KGATIOSPLSDCLTRSHSIPOANRSPILP IAKVSPSPISPIRYLUTRVLPQDNSSILPAASV 1440
DB 1381 KGATIOSPLSDCLTRSHSIPOANRSPILP IAKVSPSPISPIRYLUTRVLPQDNSSILPAASV 1440
QY 1441 RKKSQVOESSHFLQCAKKNNSLAILTEMTQDQBNVSGISGTSNRYTKKYENTVLP 1500
DB 1441 RKKSQVOESSHFLQCAKKNNSLAILTEMTQDQBNVSGISGTSNRYTKKYENTVLP 1500
QY 1501 KPDLPKTSQGYELLFPVHYIYOKDELPEETSNGSPGHLDBVESSLQGTGEGAIKNEANRP 1560
DB 1501 KPDLPKTSQGYELLFPVHYIYOKDELPEETSNGSPGHLDBVESSLQGTGEGAIKNEANRP 1560
QY 1561 GVPFLVATTESSAKPPSKLDPLPLAMDNHNGTOIPKDEMKSOEKSPEKTAKKKDTLSL 1620
DB 1561 GVPFLVATTESSAKPPSKLDPLPLAMDNHNGTOIPKDEMKSOEKSPEKTAKKKDTLSL 1620
QY 1621 NACSNHIAIAINEGONKPEIYTWAKOGRTBRCLCSQNPVILKRQREITFTTLOSQOE 1680
DB 1621 NACSNHIAIAINEGONKPEIYTWAKOGRTBRCLCSQNPVILKRQREITFTTLOSQOE 1680
QY 1681 IDYDITISVEMKREDDIYDEDENQSPRSQKTRRYFTAAVERLMDYGMSSPBYLRN 1740
DB 1681 IDYDITISVEMKREDDIYDEDENQSPRSQKTRRYFTAAVERLMDYGMSSPBYLRN 1740
QY 1741 AOSGVPQFKVYFOEFTGSPLOPLVYSGELNEHLGLDPYIRAVEENIIVWRNQA 1800
DB 1741 AOSGVPQFKVYFOEFTGSPLOPLVYSGELNEHLGLDPYIRAVEENIIVWRNQA 1800
QY 1801 PYSEYSSILSYEEDQOGAEPKKNVFNKNETKYFKVYOHMAPTKDEDCAKAAYFSV 1860
DB 1801 PYSEYSSILSYEEDQOGAEPKKNVFNKNETKYFKVYOHMAPTKDEDCAKAAYFSV 1860
QY 1861 DLEKDVHSGILGILLVCHNTLNPAGHROVYQEFALFTIIDEKTSYFTENNERNCRA 1920
DB 1861 DLEKDVHSGILGILLVCHNTLNPAGHROVYQEFALFTIIDEKTSYFTENNERNCRA 1920
QY 1921 PCNTOMDPPFKENYFPAHNGYIMDTPLGVMAGQORLRWLLSMGSENEIHSIHSG 1980
DB 1921 PCNTOMDPPFKENYFPAHNGYIMDTPLGVMAGQORLRWLLSMGSENEIHSIHSG 1980
QY 1981 VFTYRKKEEYKMALVNLVPGVEFVEMLPKSAKGIWRECLIGEHLHAQSTFLVYSNKC 2040
DB 1981 VFTYRKKEEYKMALVNLVPGVEFVEMLPKSAKGIWRECLIGEHLHAQSTFLVYSNKC 2040
QY 2041 QPILGMAIGHIRDFQITAGGQYGGWAPRLARLHYSGINAWSTKEPFFSWIKVLDLAPWII 2100
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Db	2041	QTPGLMAGSHIRDFQITASGCGMAPKRLARLHSGSINAMSTKEPSPWIKVDLAPMI	2100
Qy	2101	HGHTGCAARKFSKSLYSQIFIMYSLUGKKWQYRNSNGTLMFPKFNSSGSKHNLEN	2160
Db	2101	HGHTGCAARKFSKSLYSQIFIMYSLUGKKWQYRNSNGTLMFPKFNSSGSKHNLEN	2160
Qy	2161	PRITARIRLHPHYSINSTLMELMCCDINSCSMPFLGMSKASISDAQITASSYFTNMFA	2220
Db	2161	PRITARIRLHPHYSINSTLMELMCCDINSCSMPFLGMSKASISDAQITASSYFTNMFA	2220
Qy	2221	TWSPSKARLHLQGRSNAMRPQVNNPKEMLQVDFQKTMKYTGVTYQGVKSLTSMYKEFL	2280
Db	2221	TWSPSKARLHLQGRSNAMRPQVNNPKEMLQVDFQKTMKYTGVTYQGVKSLTSMYKEFL	2280
Qy	2281	ISSSDGHWTLTFQNGKVKYVQGNODSFTPVVNSLDPRLTRYLRIRHPSWVHQTALRM	2340
Db	2281	ISSSDGHWTLTFQNGKVKYVQGNODSFTPVVNSLDPRLTRYLRIRHPSWVHQTALRM	2340
Qy	2341	EVLGCEADQLY 2351	
Db	2341	EVLGCEADQLY 2351	
RESULT 82			
AA	AM13496		
ID	AA	AM13496 standard; Protein; 2351 AA.	
AC	AA	AM13496;	
DT	03-DEC-1997	(first entry)	
XX	Factor VII:C (Arg1689Lys).		
DE	Factor VII:C (Arg1689Lys).		
XX	Factor VII:C; analogue; substitution; Factor VIII:C deficiency;		
KW	mammal; haemophilia A.		
XX	Homo sapiens.		
OS			
FM	Key	Location/Qualifiers	
FT	Misc-difference 1708		
FT	/Label= Arg1689Lys		
PN	WO9703194-A1.		
PD	30-JAN-1997.		
XX	09-JUL-1996;	96MO-US11441.	
XX	11-JUL-1995;	95US-0001029.	
PA	(CHIR ) CHIRON CORP.		
FI	Burke RL, Rosenberg S;		
DR	WPI; 1997-119049/11.		
DR	N-PSDB; AAT61548.		
XX	Factor VIII:C analogue with Arg 1689 substituted by Lys - useful for		
PT	preventing and treating a Factor VIII:C deficiency, particularly		
XX	hemophilia A		
PS	Claim 1; Page -: 46pp; English.		
CC	This sequence represents an active Factor VIII:C polypeptide analogue.		
CC	The analogue comprises a native Factor VIII:C polypeptide that is		
CC	modified by substitution of the Arg residue at position 1689 with		
CC	Lys. The polypeptide analogue can be used to prevent and treat a		
CC	Factor VIII:C deficiency in a mammal, esp. haemophilia A. This		
CC	sequence is not given in the specification and is based on the		
CC	sequence given in Genbank Ref. K01740.		
XX	Sequence 2351 AA;		
XX			

Query Match	99.9%	Score 12402	DB 18	Length 2351
Best Local Similarity	99.9%	Pred. No. 0		
Matches 2348:	Conservative	2	Mismatches	1
			Indels	0
			Gaps	0
QY	1	MOLEISNCFCLLRPCPSARRRYVIGANVLSMDVMOSDAGEIPVQARPPVPKSPFN	60	
DB	1	MOLEISNCFCLLRPCPSATRRYVIGANVLSMDVMOSDAGEIPVQARPPVPKSPFN	60	
QY	61	TSVYVKKTLVEFTHLEFNIAKPRPPMGLGPTIOAEVDTVTYILKNASHPVSLHAY	120	
DB	61	TSVYVKKTLVEFTHLEFNIAKPRPPMGLGPTIOAEVDTVTYILKNASHPVSLHAY	120	
QY	121	GVSYWKADEGAEYDQOTQOREKEDDKVFQGGSHYTVMOVLKENGPMASDPLCTVSYLSH	180	
DB	121	GVSYWKADEGAEYDQOTQOREKEDDKVFQGGSHYTVMOVLKENGPMASDPLCTVSYLSH	180	
QY	181	VDLKVQDLSGLLGVREGSLAKKETOTRLKHFLLPAVDECKSMHSEKNSLMQORD	240	
DB	181	VDLKVQDLSGLLGVREGSLAKKETOTRLKHFLLPAVDECKSMHSEKNSLMQORD	240	
QY	241	AASRAAPKMHVNVGYNRSRLPGLICGHKSYVMYVIGMGTTPRVHSIFLEGHTFLVYRNH	300	
DB	241	AASRAAPKMHVNVGYNRSRLPGLICGHKSYVMYVIGMGTTPRVHSIFLEGHTFLVYRNH	300	
QY	301	ROASLETSPITLHQAOTLLMDLGOFLFLCHISSHQHDGMEAYVYVDSCPREPOLRKKNNE	360	
DB	301	ROASLETSPITLHQAOTLLMDLGOFLFLCHISSHQHDGMEAYVYVDSCPREPOLRKKNNE	360	
QY	361	EAEYDDDLTDEMDVYFRDDNSPSFIQIRSYAKKHKPKYVHWYIAAEEBDMQYAPVLYA	420	
DB	361	EAEYDDDLTDEMDVYFRDDNSPSFIQIRSYAKKHKPKYVHWYIAAEEBDMQYAPVLYA	420	
QY	421	PDDRSYSQYQTLNNGPQIRGKRYKKVRFPMATDTETFKTEBAIOHESGLIGLVLGEYGDTL	480	
DB	421	PDDRSYSQYQTLNNGPQIRGKRYKKVRFPMATDTETFKTEBAIOHESGLIGLVLGEYGDTL	480	
QY	481	LITKKNASPRVYVPHGTDVPRVLSRRLPKGVNKLMDQFLLEGELFEKKKMYVEDQSP	540	
DB	481	LITKKNASPRVYVPHGTDVPRVLSRRLPKGVNKLMDQFLLEGELFEKKKMYVEDQSP	540	
QY	541	TKSDPRCLTRYVSSFPNNEBDLASGLIGPRLCTYKESVDQRONDMSDKRNVTLFSVEDE	600	
DB	541	TKSDPRCLTRYVSSFPNNEBDLASGLIGPRLCTYKESVDQRONDMSDKRNVTLFSVEDE	600	
QY	601	NRSYVLENIQORLPVPAQVQLEDPEFQANINHSINGVYFDSIQLSVYCHEAVYVYILS	660	
DB	601	NRSYVLENIQORLPVPAQVQLEDPEFQANINHSINGVYFDSIQLSVYCHEAVYVYILS	660	
QY	661	IGAOTDLSVFEFGYEFKKHMYEDTLTLPSPGSEVFMENBGMLTLCCHNSDPRNG	720	
DB	661	IGAOTDLSVFEFGYEFKKHMYEDTLTLPSPGSEVFMENBGMLTLCCHNSDPRNG	720	
QY	721	MTFALLKVSQDKMTGYVEDSYEDISAVYLLSKNNAIEPSSQNSRHPSTRQCFNATTI	780	
DB	721	MTFALLKVSQDKMTGYVEDSYEDISAVYLLSKNNAIEPSSQNSRHPSTRQCFNATTI	780	
QY	781	PENDIEKTDPEFAHROPKIQONVSSSDLMALLROSPTPHGSLSDIQEAKYETPSDDPS	840	
DB	781	PENDIEKTDPEFAHROPKIQONVSSSDLMALLROSPTPHGSLSDIQEAKYETPSDDPS	840	
QY	841	PGALDSNNLSSEMTJHRPQJLHNSGDMVFTEPSQIQJRLNEKLGTTAATTEAKKIDFVYSST	900	
DB	841	PGALDSNNLSSEMTJHRPQJLHNSGDMVFTEPSQIQJRLNEKLGTTAATTEAKKIDFVYSST	900	
QY	901	SNNLISITIPEDNLAAGTQNTSGLSPSPMYPHYOSQDPTLFGKSSPPLTSSGGPLSLSE	960	
DB	901	SNNLISITIPEDNLAAGTQNTSGLSPSPMYPHYOSQDPTLFGKSSPPLTSSGGPLSLSE	960	
QY	961	NNDSKLLSEGLNMSQSSMGKNVSSTSBGLFEGKRAHROPALTRKDNALRKVYSILTKTN	1020	
DB	961	NNDSKLLSEGLNMSQSSMGKNVSSTSBGLFEGKRAHROPALTRKDNALRKVYSILTKTN	1020	

Qy	1021	TSUNSNKSTNKRTHIOEPSLLEJENSPWOMUJLESDDEPKKATPLIHHRMLMDKNATLRL	1080
Dp	1021	KTSUNSNKSTNKRTHIOEPSLLEJENSPWOMUJLESDDEPKKATPLIHHRMLMDKNATLRL	1080
Qy	1081	NHMSNKTTSSKNMKNEMOQKEGPRPRAOQPMDSPFKKIPLPESARBDIOJTHCKNSJNSG	11400
Dp	1081	NHMSNKTTSSKNMKNEMOQKEGPRPRAOQPMDSPFKKIPLPESARBDIOJTHCKNSJNSG	11400
Qy	1141	QGSPEKQVSLGPEKSVBQSNFLEKKRVVYGKEFTKQVGLKEMVPESSRLJFTNLND	1200
Dp	1141	QGSPEKQVSLGPEKSVBQSNFLEKKRVVYGKEFTKQVGLKEMVPESSRLJFTNLND	1200
Qy	1201	LHENNTNNOEKKJQOEIEBEKKEKTLJQENVLPOJHTYTGTGNKFMNLEJLJSTRONVGSYD	1260
Dp	1201	LHENNTNNOEKKJQOEIEBEKKEKTLJQENVLPOJHTYTGTGNKFMNLEJLJSTRONVGSYE	1260
Qy	1261	GAYAPVJQDPERSLNDSNTNKKHTAHFSKKGEEENLEGJAGNOTQOJYEKACTRISPT	1320
Dp	1261	GAYAPVJQDPERSLNDSNTNKKHTAHFSKKGEEENLEGJAGNOTQOJYEKACTRISPT	1320
Qy	1321	SOONPVORBKALQOFPLPEJELBEKRLIYNDSJTOQSKNMKHLPSLNOJDNKE	1380
Dp	1321	SOONPVORBKALQOFPLPEJELBEKRLIYNDSJTOQSKNMKHLPSLNOJDNKE	1380
Qy	1381	KGALTQSPSLDCLTRHSHIPOANRSPPLIAKVSFSPISIRPLTRVLJFODNSHLPASY	1440
Dp	1381	KGALTQSPSLDCLTRHSHIPOANRSPPLIAKVSFSPISIRPLTRVLJFODNSHLPASY	1440
Qy	1441	RKKSQGOESHSPLQCAKKNMNLJALITLMTDQJREVSJLQTSNTSVYKKEVETVPL	1500
Dp	1441	RKKSQGOESHSPLQCAKKNMNLJALITLMTDQJREVSJLQTSNTSVYKKEVETVPL	1500
Qy	1501	KPDLPKTSQGVLEPLPVHJHYOKLPEJTEGNSPGHLDJVESJLLOGDEAIKWNPAMP	1560
Dp	1501	KPDLPKTSQGVLEPLPVHJHYOKLPEJTEGNSPGHLDJVESJLLOGDEAIKWNPAMP	1560
Qy	1561	GKVPFLVAPRESSAKPRPSLIDPLAMNHNJCPIOPEEMKSOEKSPEKTPAFKKDITLJL	1620
Dp	1561	GKVPFLVAPRESSAKPRPSLIDPLAMNHNJCPIOPEEMKSOEKSPEKTPAFKKDITLJL	1620
Qy	1621	NACSNHNAIAINEGONKEJELVTYMAQOGRTEBULGSQNPVLAKRHOIRETRTLOSQOE	1680
Dp	1621	NACSNHNAIAINEGONKEJELVTYMAQOGRTEBULGSQNPVLAKRHOIRETRTLOSQOE	1680
Qy	1681	IDYDITISVEMKKEDEJDIYDEENQSPRSQOKTRIFYTAAVERLMDYGMSSSPHLNR	1740
Dp	1681	IDYDITISVEMKKEDEJDIYDEENQSPRSQOKTRIFYTAAVERLMDYGMSSSPHLNR	1740
Qy	1741	AQSGSVQPFKKVYVQOFTQSGFTQPIVIRGELNHLJLLEPTRYBRAVEDNIMVFFRNOAR	1800
Dp	1741	AQSGSVQPFKKVYVQOFTQSGFTQPIVIRGELNHLJLLEPTRYBRAVEDNIMVFFRNOAR	1800
Qy	1801	PYSSTYSLJSEEDQOQAGEPKKNVKNPEKTIYFKVONHMAAPKDFOCKMAAFESV	1860
Dp	1801	PYSSTYSLJSEEDQOQAGEPKKNVKNPEKTIYFKVONHMAAPKDFOCKMAAFESV	1860
Qy	1861	DLEKDVHSLGJLPLVCHNNTLNPAGROYTQVEJALFTJEDTKSWYFLENMERCA	1920
Dp	1861	DLEKDVHSLGJLPLVCHNNTLNPAGROYTQVEJALFTJEDTKSWYFLENMERCA	1920
Qy	1921	PCNLIQMDPEFKKNYFFAHJINGYIMDLJCLJVAQOQIRJRWJLSMGSNENISIHFSH	1980
Dp	1921	PCNLIQMDPEFKKNYFFAHJINGYIMDLJCLJVAQOQIRJRWJLSMGSNENISIHFSH	1980
Qy	1981	VYTRAKKEEKMAJLYLYGVEFEYEMJPKASIMVBEJLJSEHJHAGMSTFLVJYSSNC	2040
Dp	1981	VYTRAKKEEKMAJLYLYGVEFEYEMJPKASIMVBEJLJSEHJHAGMSTFLVJYSSNC	2040
Qy	2041	QTPJGMAHSGHTRPQJTTASGQYQWAPRLARLHSSJNASTKEPPSPWIKVDLAPMII	2100
Dp	2041	QTPJGMAHSGHTRPQJTTASGQYQWAPRLARLHSSJNASTKEPPSPWIKVDLAPMII	2100
Qy	2101	HKIKQAGARFSSJLISQFIIMYSJLQKWKQYTRYRNSJTGJLMEFEGVJSSGJIKINIFN	2160

Db	2101	HGICGQARGCKSFSSLYISQITIMYSLDGCKWQTYRGRNSGTLAMFPGFNVDSSIKINIFEN	2160
Qy	2161	PTIARIYRIHLPHYHSISFSTLRAMELMGCDLNSGMDLMEKSAISDQIYASSYFNHFA	2220
Db	2161	PTIARIYRIHLPHYHSISFSTLRAMELMGCDLNSGMDLMEKSAISDQIYASSYFNHFA	2220
Qy	2221	TWSSSKARLHLGGRSNARPOVNNPKRELDVDPQKTKYGTCTGQYKSLTSMYKKEFL	2280
Db	2221	TWSSSKARLHLGGRSNARPOVNNPKRELDVDPQKTKYGTCTGQYKSLTSMYKKEFL	2280
Qy	2281	ISSSQDSDHMTLEFONGKVKYFGQGNDSFTPVVNSLDPLRLIRLHPQSWYHQIALRM	2340
Db	2281	ISSSQDSDHMTLEFONGKVKYFGQGNDSFTPVVNSLDPLRLIRLHPQSWYHQIALRM	2340
Qy	2341	EVLCGEADQDLY 2351	
Db	2341	EVLCGEADQDLY 2351	
RESULT 83			
ID	AAV21676	AAV21676 standard; Protein; 2351 AA.	
AC	AAV21676;		
DT	18-AUG-1999	(first entry)	
DE	Factor VIII protein full length sequence.		
KM	Factor VIII protein; gene modification; gene therapy; clinical disorder;		
KW	splicing pattern; RNA processing; gene regulation; beta-domain; human.		
OS	Homo sapiens.		
PN	W099292848-A1.		
PD	17-JUN-1999.		
PF	25-NOV-1998;	98MO-US25354.	
PR	16-JAN-1998;	980US-0071596.	
PR	05-DEC-1997;	970US-0067614.	
PA	(IMMU-) IMMUNE RESPONSE CORP.		
PI	Bidlingmaier S, Gonzales JEN, Ill CR, Yang CO;		
DR	WPI; 1999-385602/32.		
DR	N-PSDB; AAX82261.		
PT	Genes and vectors exhibiting increased expression and novel splicing		
PT	patterns, useful for expression of, e.g. beta-domain deleted factor		
PT	VIII		
PS	Example 1; Page 101-115; 123pp; English.		
CC	The invention describes novel genes and vectors exhibiting increased		
CC	expression and novel splicing patterns. It provides a gene encoding a		
CC	Factor VIII protein, that comprises one or more consensus or near		
CC	consensus splice sites which have been corrected to increase expression.		
CC	The method, DNA sequences and expression vectors can be used to increase		
CC	the expression of a gene, especially a Factor VIII gene. Genes containing		
CC	modified 5' and/or 3' untranslated regions have optimized expression		
CC	levels and tissue-specific expression. The methods are used for		
CC	identification and correction of consensus splice sites, addition of		
CC	introns, optimization of 5' and 3' untranslated regions and increase in		
CC	cytoplasmic RNA accumulation. Hence the DNAs are useful in gene therapy		
CC	to treat a clinical disorder, to study RNA processing and/or gene		
CC	regulation. The present sequence represents the full length factor VIII		
CC	protein (construct pLZ-6).		
XX	Sequence 2351 AA;		
XX			

Query Match	99.98;	Score 12402;	DB 20;	Length 2351;
Best Local Similarity	99.98;	Pred. No. 0;		
Matches 2348;	Conservative 2;	Mismatches 1;	Indels 0;	Gaps 0;
Qy	1	MOIELSTCFELCLLRCEFSATRRYYLGAVELSMYDOSDLGELVPDARPPRVKSPFFN	60	
Db	1	MEIELSTCFELCLLRCEFSATRRYYLGAVELSMYDOSDLGELVPDARPPRVKSPFFN	60	
Qy	61	TSVYVKKTLPEVEFDHLEFNAPRPMPMGLGPTIOAEVYDVTYITLKMAHSYSLHAY	120	
Db	61	TSVYVKKTLPEVEFDHLEFNAPRPMPMGLGPTIOAEVYDVTYITLKMAHSYSLHAY	120	
Qy	121	GVSYKASGEAEVDQTSQREKEDKVPFGGSHTYVQVILKENGPAADPLCTLYSLSH	180	
Db	121	GVSYKASGEAEVDQTSQREKEDKVPFGGSHTYVQVILKENGPAADPLCTLYSLSH	180	
Qy	181	VDLVKDLNSGLIGALLVCREGSLAEKQTLHKEILLFAVEDGKSMHSETKNSLMDRD	240	
Db	181	VDLVKDLNSGLIGALLVCREGSLAEKQTLHKEILLFAVEDGKSMHSETKNSLMDRD	240	
Qy	241	AASARAMPKMTVNGVYNSRLPGLIGCHRSKVYWHVIGMGTPEVHSIFLEGHTFLVRNH	300	
Db	241	AASARAMPKMTVNGVYNSRLPGLIGCHRSKVYWHVIGMGTPEVHSIFLEGHTFLVRNH	300	
Qy	301	ROASLESPIITFLAOTLLMDLGOFLFCCHSHSQHDGMAAYKVDSCPEPQLMKANE	360	
Db	301	ROASLESPIITFLAOTLLMDLGOFLFCCHSHSQHDGMAAYKVDSCPEPQLMKANE	360	
Qy	361	EAEDYDDDLTDSEMDVVRFDODNSPSFQIQRSAVKKRPKTWVHYIAAEEDMDVAPVLA	420	
Db	361	EAEDYDDDLTDSEMDVVRFDODNSPSFQIQRSAVKKRPKTWVHYIAAEEDMDVAPVLA	420	
Qy	421	PDORSYKSOYLNNGPORIGKRYKRVPMAYTDEFKTRALIOHESITLIGPLLYGVGDTL	480	
Db	421	PDORSYKSOYLNNGPORIGKRYKRVPMAYTDEFKTRALIOHESITLIGPLLYGVGDTL	480	
Qy	481	LIIFFKNOASRPYNIYPGIDTVARPLYSRRLKRYKHLKDPILLPGITFKYKWTYVEDCP	540	
Db	481	LIIFFKNOASRPYNIYPGIDTVARPLYSRRLKRYKHLKDPILLPGITFKYKWTYVEDCP	540	
Qy	541	TKSDPRCLTRYSSSFVNMERDLASGLIGPLLYCKESVDORGNOIMSDKRNVIJFSVDE	600	
Db	541	TKSDPRCLTRYSSSFVNMERDLASGLIGPLLYCKESVDORGNOIMSDKRNVIJFSVDE	600	
Qy	601	NRSWTLENIORFLPNAGVQLEDPFOASNMHSINGVYFDSLOVCLHEVAYWTLS	660	
Db	601	NRSWTLENIORFLPNAGVQLEDPFOASNMHSINGVYFDSLOVCLHEVAYWTLS	660	
Qy	661	IGAQDFLSVFSGTYTKHAKMYEDTLTFPESGETVPMSEMPGLMILGCHNSDFRNKG	720	
Db	661	IGAQDFLSVFSGTYTKHAKMYEDTLTFPESGETVPMSEMPGLMILGCHNSDFRNKG	720	
Qy	721	MTALLKVSQCDKNTGDYEDSYEDISAYLLSKNNAIEPRSFSONSRHPSTROKOPNATTI	780	
Db	721	MTALLKVSQCDKNTGDYEDSYEDISAYLLSKNNAIEPRSFSONSRHPSTROKOPNATTI	780	
Qy	781	PENDIEKTDPMFAHRTMPKIQVNSSDMLMLKOSPPTPHGLSLSDLOAKETSDOPS	840	
Db	781	PENDIEKTDPMFAHRTMPKIQVNSSDMLMLKOSPPTPHGLSLSDLOAKETSDOPS	840	
Qy	841	PGALDSNNLSLEMTNHPROLHSHGDMVTFPESGQLRLNKEKLDGTATATLKLKLDKVSST	900	
Db	841	PGALDSNNLSLEMTNHPROLHSHGDMVTFPESGQLRLNKEKLDGTATATLKLKLDKVSST	900	
Qy	901	SNNLSTIPSDNLAAGTDNNTSLGPPSMVHYDSQDLYTLFGKSSPRLTESGGPRLSLEE	960	
Db	901	SNNLSTIPSDNLAAGTDNNTSLGPPSMVHYDSQDLYTLFGKSSPRLTESGGPRLSLEE	960	
Qy	961	NNDKSLTESGLMNSQESMCKNVSTESGRLFKGRRAHGRLITKONALFKYISILKTN	1020	
Db	961	NNDKSLTESGLMNSQESMCKNVSTESGRLFKGRRAHGRLITKONALFKYISILKTN	1020	

Qy	1021	KTSNNSAFNRKTHIDPRLIENSFWONILSDPEFKKVTPLTHDBMLDKMATAALRL	1080	
Db	1021	KTSNNSAFNRKTHIDPRLIENSFWONILSDPEFKKVTPLTHDBMLDKMATAALRL	1080	
Qy	1081	NHMSNKTSSKNMENVQAKKEGPIPPDAQNDPMSFFKMLPLESARWIORTHGKNSLNSG	1140	
Db	1081	NHMSNKTSSKNMENVQAKKEGPIPPDAQNDPMSFFKMLPLESARWIORTHGKNSLNSG	1140	
Qy	1141	OGSPKQVLSIGPEKSVGEONFLSEKKNVYVGGEFTKQVGLKEVFPSSNLFJTNLDN	1200	
Db	1141	OGSPKQVLSIGPEKSVGEONFLSEKKNVYVGGEFTKQVGLKEVFPSSNLFJTNLDN	1200	
Qy	1201	LHENNTNOKKTOEILEKKEFTLQENNVLPQIHYTGKRNKRLFLISTRQVNVESVD	1260	
Db	1201	LHENNTNOKKTOEILEKKEFTLQENNVLPQIHYTGKRNKRLFLISTRQVNVESVD	1260	
Qy	1261	GATAPVLQDFRSINDSTNFKKHTAHFSKQGEENLEGJNOTKOIVERVACTRISPNPT	1320	
Db	1261	GATAPVLQDFRSINDSTNFKKHTAHFSKQGEENLEGJNOTKOIVERVACTRISPNPT	1320	
Qy	1321	SQONFVQORSKRALKQFRLPLEETELEKRIIVDQTSQMSKMKHLFSTLTQIDYNEKE	1380	
Db	1321	SQONFVQORSKRALKQFRLPLEETELEKRIIVDQTSQMSKMKHLFSTLTQIDYNEKE	1380	
Qy	1381	KGATQSPISDCLTRBSHTPOANBSPLIAVSPFSIRPILTVFLPQDSSHLPAASY	1440	
Db	1381	KGATQSPISDCLTRBSHTPOANBSPLIAVSPFSIRPILTVFLPQDSSHLPAASY	1440	
Qy	1441	RKDSGVOESSHFLQAKKNNLSLILTEMTGQDREVSIGTSATNSVYKKEVNTLP	1500	
Db	1441	RKDSGVOESSHFLQAKKNNLSLILTEMTGQDREVSIGTSATNSVYKKEVNTLP	1500	
Qy	1501	KPDLPKTSQAVELLPVHYIYOKDLPPTSGPSGHLIDVBSLQGTGEGAIKKNENMRP	1560	
Db	1501	KPDLPKTSQAVELLPVHYIYOKDLPPTSGPSGHLIDVBSLQGTGEGAIKKNENMRP	1560	
Qy	1561	GVPPFLKATIESAKTPSKLDPRLAMDHYGTQIPREBKSOEKSPERTAKKODTLLS	1620	
Db	1561	GVPPFLKATIESAKTPSKLDPRLAMDHYGTQIPREBKSOEKSPERTAKKODTLLS	1620	
Qy	1621	NACESNHAIAINEGONKPEIEVTYAKOGERTLCSQNPVLRKHQREITRTYLOSQOE	1680	
Db	1621	NACESNHAIAINEGONKPEIEVTYAKOGERTLCSQNPVLRKHQREITRTYLOSQOE	1680	
Qy	1681	IDYDQTSVEMKKEDPDIDEDENQSPRSFQKTRHYFIYAVERLMDYGMSSSPHYLRNR	1740	
Db	1681	IDYDQTSVEMKKEDPDIDEDENQSPRSFQKTRHYFIYAVERLMDYGMSSSPHYLRNR	1740	
Qy	1741	AOSGSVPOFKKVVFOERTDGSFTQPLYKGBLBNHGLGFTYLAEBEDNIWTRMNASR	1800	
Db	1741	AOSGSVPOFKKVVFOERTDGSFTQPLYKGBLBNHGLGFTYLAEBEDNIWTRMNASR	1800	
Qy	1801	PYSFYSSLISYEDDQOGAEPKRNKVFKNETKTYFMKVQHMAPTKDEPDKAMAYFSDV	1860	
Db	1801	PYSFYSSLISYEDDQOGAEPKRNKVFKNETKTYFMKVQHMAPTKDEPDKAMAYFSDV	1860	
Qy	1861	DLEKDVHSGGLGPLVCHNTNLPNAGQVYVQEFALFETPDETKSYFTJENNERNCRA	1920	
Db	1861	DLEKDVHSGGLGPLVCHNTNLPNAGQVYVQEFALFETPDETKSYFTJENNERNCRA	1920	
Qy	1921	PCNIDMEDPTEKERTFRHAINGIIMDTLGLYMAQODRIKWLILSGNSNENIHSIHSGH	1980	
Db	1921	PCNIDMEDPTEKERTFRHAINGIIMDTLGLYMAQODRIKWLILSGNSNENIHSIHSGH	1980	
Qy	1981	VETVARKKEEKMALYNLYPGVEVEYEMLPKSAGITWRVECLIGBHLAAGSTLFLVYSNKC	2040	
Db	1981	VETVARKKEEKMALYNLYPGVEVEYEMLPKSAGITWRVECLIGBHLAAGSTLFLVYSNKC	2040	
Qy	2041	QTPPLMAGHTRPQUTASAGQYQMAAPLALRHSIGSINAMSTKEPFWSMIVVDLAPMI	2100	
Db	2041	QTPPLMAGHTRPQUTASAGQYQMAAPLALRHSIGSINAMSTKEPFWSMIVVDLAPMI	2100	
Qy	2101	HGIKTQGARQKFSKVIISQIIMYSLDCKKQTYRGNSIGTLMVFFGVNDSGKIHIFN	2160	

Db	2101	HGIRKQAGRKQFSSLSYSQFIIMYSLSGKKMQYRNSGTGLMVFEGVDSGSKHNIFN	2160
Qy	2161	PIPIARIYRLHPHYRISRTLMELMGCDLNSCSMPLGEMSKAISDAQITASSYFTMFA	2220
Db	2161	PIPIARIYRLHPHYRISRTLMELMGCDLNSCSMPLGEMSKAISDAQITASSYFTMFA	2220
Qy	2221	TWSPSKARHLQGRSNAMRPQVNNPKEMLOYDQKTKMYGTGTTGGVSLTSMYKEFL	2280
Db	2221	TWSPSKARHLQGRSNAMRPQVNNPKEMLOYDQKTKMYGTGTTGGVSLTSMYKEFL	2280
Qy	2281	ISSSDGQHWTLTFQNGKVKVEQGNDSFTPVVNSLDPLRLRYLRHPOSVMHQIALRM	2340
Db	2281	ISSSDGQHWTLTFQNGKVKVEQGNDSFTPVVNSLDPLRLRYLRHPOSVMHQIALRM	2340
Qy	2341	EVLGCEAODLY 2351	
Db	2341	EVLGCEAODLY 2351	
RESULT 84			
AAW10592	standard; protein; 2351 AA.		
AAW10592;			
03-DEC-1997	(first entry)		
Factor VIII:C (Tyr1786His).			
Factor VIII:C; F8C; Factor V A; Factor V C; domain; F8C deficiency;			
haemophilia A; blood clotting disorder; immunogen; antibody.			
Homo sapiens.			
Key	Location/Qualifiers		
Peptide	1..19		
Protein	/note="Signal peptide"		
Misc-difference	/note="Mature factor VIII:C"		
	/label= Tyr1786His		
MO9703191-A1.			
30-JAN-1997.			
28-JUN-1996;	96MO-US11013.		
11-JUL-1995;	95US-0001030.		
(CHIR ) CHIRON CORP.			
Hung DT;			
WPI: 1997-119047/11.			
Factor VIII:C analogue - modified to comprise Factor V A or C domain			
or subdomain, for increased stability or activity			
Claim 6; Page -: 45pp; English.			
The sequences given in W10590-92 represent active Factor VIII:C (F8C)			
polypeptide analogues. These analogues comprises a native F8C			
polypeptide modified to comprise the presence of a Factor V A and/or			
C domain and/or subdomain. The F8C polypeptide analogues, alone or in			
combination, can be used for the prevention or treatment of an active			
F8C deficiency, i.e. haemophilia A and other blood clotting disorders.			
The analogue can also be used as an immunogen for antibody production.			
The analogues can have an increased plasma half-life, or specific			
activity. This sequence is not given in the specification and is			
based on the sequence derived from Genbank ref. K01740.			
Seq	Sequence	2351 AA:	
Query Match	99.9%;	Score 12400;	DB 18; Length 2351;
Best Local Similarity	99.9%;	Pred. No. 0;	
Matches 2248;	Conservative	2; Mismatches	1; Indels 0; Gaps 0;
Qy	1	MOIELSTCFCLLRPCFSARRYLYGAVELSDMYQNSDLGELPVDARPPRPKSPFN	60
Db	1	MOIELSTCFCLLRPCFSATRRYLYGAVELSDMYQNSDLGELPVDARPPRPKSPFN	60
Qy	61	TSVYKKTLEFEETHLENIAKPRPMGLGPTDAEYDTPVYTLKNAASHVSLAHV	120
Db	61	TSVYKKTLEFEETHLENIAKPRPMGLGPTDAEYDTPVYTLKNAASHVSLAHV	120
Qy	121	GVSYWKASGEAEYDDQTSQREKEDKVPFGSHTYVQYALKENGPMSADPLCLTYSLSH	180
Db	121	GVSYWKASGEAEYDDQTSQREKEDKVPFGSHTYVQYALKENGPMSADPLCLTYSLSH	180
Qy	181	VDLYKDLNSGLIGALLVCEGSLAKERTQTLHKFILLFVPEDEKSMHSETKNSLMODRD	240
Db	181	VDLYKDLNSGLIGALLVCEGSLAKERTQTLHKFILLFVPEDEKSMHSETKNSLMODRD	240
Qy	241	AASARAMPKMTYNGVYKNSLPLGLGCHKSVYWHYIGCTTPEVHSIFLEGGTFLYRNH	300
Db	241	AASARAMPKMTYNGVYKNSLPLGLGCHKSVYWHYIGCTTPEVHSIFLEGGTFLYRNH	300
Qy	301	ROASTESPTLFTLAOTLMDLQGFLLFCHISSHODGMEAVYKVDSCPEPQLRMKNE	360
Db	301	ROASTESPTLFTLAOTLMDLQGFLLFCHISSHODGMEAVYKVDSCPEPQLRMKNE	360
Qy	361	EAEYDDDLTDSMDVYRPPDONSPTFOIRSAKKHPRTWYHYIAAEEDMDYAPLYLA	420
Db	361	EAEYDDDLTDSMDVYRPPDONSPTFOIRSAKKHPRTWYHYIAAEEDMDYAPLYLA	420
Qy	421	PDDRSYKSOYLNNGPORIGRKYKVKVREMAATDETETREAIQHEGSLIGLILGEGDTL	480
Db	421	PDDRSYKSOYLNNGPORIGRKYKVKVREMAATDETETREAIQHEGSLIGLILGEGDTL	480
Qy	481	LIIFRNQASRPYNIYHGTIDVRLPYLSRLPKGVKHLKDFPLPELPIFYKYFWYVEDGQ	540
Db	481	LIIFRNQASRPYNIYHGTIDVRLPYLSRLPKGVKHLKDFPLPELPIFYKYFWYVEDGQ	540
Qy	541	TKSDPRLCTRYSSFVNNMRDLASGLIPLLCYKESVDQGNQJMSDKRVLLFSYFDE	600
Db	541	TKSDPRLCTRYSSFVNNMRDLASGLIPLLCYKESVDQGNQJMSDKRVLLFSYFDE	600
Qy	601	NRSWYLTENIQRLPNPAGVQLEDEPEQASINMHSINGYVFDLSQLSVCLHEVAYWYIIS	660
Db	601	NRSWYLTENIQRLPNPAGVQLEDEPEQASINMHSINGYVFDLSQLSVCLHEVAYWYIIS	660
Qy	661	IGAOTDFLSYFSGYTFKHKMYEDDTLTLPFSGEYVPMSEMENPGLMTLGCNDSDFRNKQ	720
Db	661	IGAOTDFLSYFSGYTFKHKMYEDDTLTLPFSGEYVPMSEMENPGLMTLGCNDSDFRNKQ	720
Qy	721	MTALLKVSQCDKNTGTYEDSTEDISAILLSKNNALIEPSPQNSRRHSTKQKFNATTT	780
Db	721	MTALLKVSQCDKNTGTYEDSTEDISAILLSKNNALIEPSPQNSRRHSTKQKFNATTT	780
Qy	781	PENDIEKTDPMFAHRTPMKIQNVSSDQLMLRKQSPPHGLSLSDLOEAKYETFSDDPS	840
Db	781	PENDIEKTDPMFAHRTPMKIQNVSSDQLMLRKQSPPHGLSLSDLOEAKYETFSDDPS	840
Qy	841	PGALDSNNSTSEMTTHRPOLHSGDMVTTPSSGIQRLMEKIGTAAATELKKLDFKYSST	900
Db	841	PGALDSNNSTSEMTTHRPOLHSGDMVTTPSSGIQRLMEKIGTAAATELKKLDFKYSST	900
Qy	901	NNILISTIPSDNIAAGTDWTSGLGPPSPVHYSDLDITLTFKSKSSPLTEGGGLSIEE	960
Db	901	NNILISTIPSDNIAAGTDWTSGLGPPSPVHYSDLDITLTFKSKSSPLTEGGGLSIEE	960
Qy	961	NNDSKLESGIMNSQSSGKAVSSTEGSRFLFGKGRAPALTLTKDMLFVYSISLTKTN	1020
Db	961	NNDSKLESGIMNSQSSGKAVSSTEGSRFLFGKGRAPALTLTKDMLFVYSISLTKTN	1020

```

QY 1021 KTSNNSATNRKTHIDPSLLIENSPYMONILESDPEFKVTPLIHDMELMDKNAATRL 1080
    |||||||
Db 1021 KTSNNSATNRKTHIDPSLLIENSPYMONILESDPEFKVTPLIHDMELMDKNAATRL 1080
QY 1081 NMSNKTSSKKNMXYOQKKBGP1PPDAONPDMSFFKMLPLPESARW1QRTHGKNSLNG 1140
    |||||||
Db 1081 NMSNKTSSKKNMXYOQKKBGP1PPDAONPDMSFFKMLPLPESARW1QRTHGKNSLNG 1140
QY 1141 QGSPKOLVSLGPEKSVGEONFLSEKKNVVVGGEFTKDVGLKEVAFSSNLELTJLMD 1200
    |||||||
Db 1141 QGSPKOLVSLGPEKSVGEONFLSEKKNVVVGGEFTKDVGLKEVAFSSNLELTJLMD 1200
QY 1201 LHENNTHNOEKKIOEIEKKEKTLIOENNVLPQIHVYTGKNNKMLFTLSTRQWESVD 1260
    |||||||
Db 1201 LHENNTHNOEKKIOEIEKKEKTLIOENNVLPQIHVYTGKNNKMLFTLSTRQWESVD 1260
QY 1261 GAVAPVLQDFRSLNDSTNFKKHTAHFSKKEEENLEGLGNOTKOIVERACTTRISPNT 1320
    |||||||
Db 1261 GAVAPVLQDFRSLNDSTNFKKHTAHFSKKEEENLEGLGNOTKOIVERACTTRISPNT 1320
QY 1321 SQONFVTOQRKRALKOFLPLEETELEKRIIVDTSTOKSKNMKHLTPSTLTOTIDYNEK 1380
    |||||||
Db 1321 SQONFVTOQRKRALKOFLPLEETELEKRIIVDTSTOKSKNMKHLTPSTLTOTIDYNEK 1380
QY 1381 KGATOSP1SDCLTRSHS1POANSPLPIAKVSSFSIRPIYTLTVLEFQDNSSHLPAASV 1440
    |||||||
Db 1381 KGATOSP1SDCLTRSHS1POANSPLPIAKVSSFSIRPIYTLTVLEFQDNSSHLPAASV 1440
QY 1441 RKDGVQESSHFLQAKKNNLSLA1LTLEMTSDOREVSLGTSATNSVTKKKEENTVLP 1500
    |||||||
Db 1441 RKDGVQESSHFLQAKKNNLSLA1LTLEMTSDOREVSLGTSATNSVTKKKEENTVLP 1500
QY 1501 KPDLPTSGKVELLPVHTYOKLPEPTETNSGSGHLD1VEGSLQGEKIKKNEANRP 1560
    |||||||
Db 1501 KPDLPTSGKVELLPVHTYOKLPEPTETNSGSGHLD1VEGSLQGEKIKKNEANRP 1560
QY 1561 GKVPFLVAATESAKTPSKLDPLAMNHGTQ1PREEKSQEKPEPTAKKDOTLSL 1620
    |||||||
Db 1561 GKVPFLVAATESAKTPSKLDPLAMNHGTQ1PREEKSQEKPEPTAKKDOTLSL 1620
QY 1621 NACESNHA1A1NEGONKPEIEVTWAKOGTRERICSONPVLKRHOREITRTLOSQOE 1680
    |||||||
Db 1621 NACESNHA1A1NEGONKPEIEVTWAKOGTRERICSONPVLKRHOREITRTLOSQOE 1680
QY 1681 IDYDDTISVEMKKEDDIYDEDENOSPSPFOKTRHYFTIAAVERLMDYGSSPHVLRNR 1740
    |||||||
Db 1681 IDYDDTISVEMKKEDDIYDEDENOSPSPFOKTRHYFTIAAVERLMDYGSSPHVLRNR 1740
QY 1741 AQSQSVQFKKVVFOEFTDGSFTQPLRGELNHLGLGPYIRAEVEDN1WTFERNQASR 1800
    |||||||
Db 1741 AQSQSVQFKKVVFOEFTDGSFTQPLRGELNHLGLGPYIRAEVEDN1WTFERNQASR 1800
QY 1801 PYSFVSLISYEEDQOGAEPKKNFVAPNETKTYEFKVOHNAAPTKDEFDCKAAYFSVD 1860
    |||||||
Db 1801 PYSFVSLISYEEDQOGAEPKKNFVAPNETKTYEFKVOHNAAPTKDEFDCKAAYFSVD 1860
QY 1861 DLEKDVHSLG1PLVACHNTL1NPAHGOVYTOEFLFTIDEDKSKYFERNERNCR 1920
    |||||||
Db 1861 DLEKDVHSLG1PLVACHNTL1NPAHGOVYTOEFLFTIDEDKSKYFERNERNCR 1920
QY 1921 PCNIOMEDPTFKENYRFHAINGYIMDTLPGIYVAOOR1RWYL1SMGSEN1H1HSGH 1980
    |||||||
Db 1921 PCNIOMEDPTFKENYRFHAINGYIMDTLPGIYVAOOR1RWYL1SMGSEN1H1HSGH 1980
QY 1981 VFTVRKKEEYKMA1Y1LPGVEFETVEMLPKAGIMRVECLIGEH1HAGMSTLFLVYSNKC 2040
    |||||||
Db 1981 VFTVRKKEEYKMA1Y1LPGVEFETVEMLPKAGIMRVECLIGEH1HAGMSTLFLVYSNKC 2040
QY 2041 QTP1GMA5GH1RDP01TASG0TG0MAP1ALH1SG1NNAWSTKEPFSW1KVD1LAPM1I 2100
    |||||||
Db 2041 QTP1GMA5GH1RDP01TASG0TG0MAP1ALH1SG1NNAWSTKEPFSW1KVD1LAPM1I 2100

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QY 2101 HGITGQARQFSSLYISOFITMYS1LQKKMOTYRGNSGTGLMVEFGNVDSG1KH1FN 2160
    |||||||
Db 2101 HGITGQARQFSSLYISOFITMYS1LQKKMOTYRGNSGTGLMVEFGNVDSG1KH1FN 2160
QY 2161 PPIIARI1RLHPHYSINSTL1MELMGCDLNSGSMPLGMSKRAISDAQITASSYFTNMR 2220
    |||||||
Db 2161 PPIIARI1RLHPHYSINSTL1MELMGCDLNSGSMPLGMSKRAISDAQITASSYFTNMR 2220
QY 2221 TWSPSKARL1H0GRSNAMRPQVNNPEKMLQVDFOKTMKVTGVTQGVKSLTSMYKREFL 2280
    |||||||
Db 2221 TWSPSKARL1H0GRSNAMRPQVNNPEKMLQVDFOKTMKVTGVTQGVKSLTSMYKREFL 2280
QY 2281 ISSQDGHQWTLPEFQNGKVKYVQGNQDSFTPVNSLDPLRLR1R1HPOSVMQ1ALRM 2340
    |||||||
Db 2281 ISSQDGHQWTLPEFQNGKVKYVQGNQDSFTPVNSLDPLRLR1R1HPOSVMQ1ALRM 2340
QY 2341 EVLGCEAODLY 2351
    |||||||
Db 2341 EVLGCEAODLY 2351

RESULT 85
AAM11471
ID AAM11471 standard; Protein; 2351 AA.
AC AAM11471;
DT 21-NOV-1997 (first entry)
XX
DE Active Factor VIII:C analogue, R336X, R1719X, R1721X.
XX
KW Factor VIII:C analogue; glycoprotein; blood coagulation cascade;
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;
KW proteolytic cleavage.
OS Homo sapiens.
OS Synthetic.
XX
FH Key 1..19 Location/Qualifiers
FT Peptide /note= "signal peptide"
FT Protein 20..2350
FT Region /note= "mature Factor VIII:C"
FT 20..1667
FT /note= "heavy chain fragment"
FT Modified-site 355
FT Domain /label= Pro, Glu, Asp, Asn, Gln, Ser, Tyr
FT 759..1667
FT Region /note= "B domain"
FT 1668..2349
FT Modified-site 1738 /note= "light chain fragment"
FT FT /label= Pro, Glu, Asp, Asn, Gln, Ser, Tyr
FT Modified-site 1740
FT /label= Glu, Asp, Asn, Gln, Ser, Tyr
PN MO9703195-A1.
XX
PD 30-JAN-1997.
XX
PE 09-JUL-1996; 96WO-US11444.
XX
PR 11-JUL-1995; 95US-0001025.
XX
PA (CHIR ) CHIRON CORP.
XX
PI Cohen FE, Hung DT, Innis M:
XX
DR WPI; 1997-119050/11.
XX
PT Factor VIII:C analog modified adjacent to a non-activating Arg
PT residue - used in the treatment of haemophiliacs, by improvement of

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PT haemostasis

PS Claim 39; Page -: 90pp; English.

CC AAM1330-W1472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophilias, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.

SQ Sequence 2351 AA;

Query Match 99.9%; Score 12400; DB 18; Length 2351;

Best Local Similarity 99.9%; Pred. No. 0;

Matches 2348; Conservative 0; Mismatches 3; Indels 0; Gaps 0;

QY 1 MOELSTCFCLLRCPASATRRYYLGAVELSDMYQSDGLPDAFAFRPRVPSPPN 60  
DB 1 MOELSTCFCLLRCPASATRRYYLGAVELSDMYQSDGLPDAFAFRPRVPSPPN 60  
QY 61 TSVVYKKTLEVEFTDHLFNIAKPRPMWGLIGBTIOAEYDTVTTLKNASHPVSLAAV 120  
DB 61 TSVVYKKTLEVEFTDHLFNIAKPRPMWGLIGBTIOAEYDTVTTLKNASHPVSLAAV 120  
QY 121 GSVYWKASGAEYDDOTSOREKEDKYPGSGSHYYWQYLKENGMAADPLCTLYSLSH 180  
DB 121 GSVYWKASGAEYDDOTSOREKEDKYPGSGSHYYWQYLKENGMAADPLCTLYSLSH 180  
QY 181 VDLVKDLSGLIGALLVCBESGLAKERTQTLHKFILLPAVDEGKSWHSETKNSLMODRD 240  
DB 181 VDLVKDLSGLIGALLVCBESGLAKERTQTLHKFILLPAVDEGKSWHSETKNSLMODRD 240  
QY 241 AASARAMPKMHVNGVYVNSLPLGLIGCHRSKSVWHVIGMGTPEVHSLFTEGHTFLVRNH 300  
DB 241 AASARAMPKMHVNGVYVNSLPLGLIGCHRSKSVWHVIGMGTPEVHSLFTEGHTFLVRNH 300  
QY 301 ROASLETSPTTFLRNTTSMYDLSGFLFCHTSSHOHDGMEAVYKVDSPREPOLAKMNE 360  
DB 301 ROASLETSPTTFLRNTTSMYDLSGFLFCHTSSHOHDGMEAVYKVDSPREPOLAKMNE 360  
QY 361 EAEYDDDLTDSKMDVYRFDNDSPSFLQIRSVAKKHPRTWVHTAAEEDMDYAPLVLA 420  
DB 361 EAEYDDDLTDSKMDVYRFDNDSPSFLQIRSVAKKHPRTWVHTAAEEDMDYAPLVLA 420  
QY 421 PDDRSYKSOYLNNGPORIGRKAKVPMATYDEFTPREAIOHESGLIGPLLYGEGDTL 480  
DB 421 PDDRSYKSOYLNNGPORIGRKAKVPMATYDEFTPREAIOHESGLIGPLLYGEGDTL 480  
QY 481 LIFKKNASPRNYIYHGTIDYRPLYSRRLPKVYKHLKDFLLPELRTKRYKYVYEDGP 540  
DB 481 LIFKKNASPRNYIYHGTIDYRPLYSRRLPKVYKHLKDFLLPELRTKRYKYVYEDGP 540  
QY 541 TKSDPRCLTRYYSFVNNEBDLASGLIGPLLYCKESVDORGNQIMSDKRVILFVDE 600  
DB 541 TKSDPRCLTRYYSFVNNEBDLASGLIGPLLYCKESVDORGNQIMSDKRVILFVDE 600  
QY 601 NRSWYLFENTIOFLPAPGVOLEDPFOASINWHSINGVPSIOLSTCJHEVAVYIIS 660  
DB 601 NRSWYLFENTIOFLPAPGVOLEDPFOASINWHSINGVPSIOLSTCJHEVAVYIIS 660

DB 601 NRSWYLFENTIOFLPAPGVOLEDPFOASINWHSINGVPSIOLSTCJHEVAVYIIS 660  
QY 661 IGAOTDFLSVFSGYTERFKKMYEDTLTLPESGETVEMSMENPGLWILCCHNSDFRNG 720  
DB 661 IGAOTDFLSVFSGYTERFKKMYEDTLTLPESGETVEMSMENPGLWILCCHNSDFRNG 720  
QY 721 MTALLKSSCDKMTGDIYEDSYEDISAVYLSKNNALTEPSPFSQNSRHPSTROKOFANATTI 780  
DB 721 MTALLKSSCDKMTGDIYEDSYEDISAVYLSKNNALTEPSPFSQNSRHPSTROKOFANATTI 780  
QY 781 PENDIETDPMFNAHRTPMKPIQONVSSDMLMLROSPPHGISLSDIOEAKYETFSDDPS 840  
DB 781 PENDIETDPMFNAHRTPMKPIQONVSSDMLMLROSPPHGISLSDIOEAKYETFSDDPS 840  
QY 841 PGALDSNNSLSEMTFRPOLNHSDDVFTPESGLOLRLENEKIGTTAATELKLDIFYVSST 900  
DB 841 PGALDSNNSLSEMTFRPOLNHSDDVFTPESGLOLRLENEKIGTTAATELKLDIFYVSST 900  
QY 901 SNNLSTIPSDNLAAGTNTSILGPPMPVHYDSOLDTLTPEGKSSPLTESGGPLSLEE 960  
DB 901 SNNLSTIPSDNLAAGTNTSILGPPMPVHYDSOLDTLTPEGKSSPLTESGGPLSLEE 960  
QY 961 NNDKLLSEGLMNSQSSMGKNVSTESGRLFKGRAPRALLTKDNLFRVSIISLKTN 1020  
DB 961 NNDKLLSEGLMNSQSSMGKNVSTESGRLFKGRAPRALLTKDNLFRVSIISLKTN 1020  
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DB 1021 KTSNNSATNKRTHIDGPSLLTENSFVWONILESDTEFEKVTPLIHDRMLMDXNATYALRL 1080  
QY 1081 NNMKNKTSSKNMKNVQOKKEGPIPPAONQDMSPFKMLFLPESARMTORTHOKNSLNG 1140  
DB 1081 NNMKNKTSSKNMKNVQOKKEGPIPPAONQDMSPFKMLFLPESARMTORTHOKNSLNG 1140  
QY 1141 QGSPKOLVSLGPEKSVGONFLSEKKRVVVGGEFTYDVGLEKMEPPSSRNILFTNLDN 1200  
DB 1141 QGSPKOLVSLGPEKSVGONFLSEKKRVVVGGEFTYDVGLEKMEPPSSRNILFTNLDN 1200  
QY 1201 LHEMNTNOKKIOEIEKEKETLLOEWNVLPOLHYTVYTKNKNKMLFLSTRONVGSYD 1260  
DB 1201 LHEMNTNOKKIOEIEKEKETLLOEWNVLPOLHYTVYTKNKNKMLFLSTRONVGSYD 1260  
QY 1261 GAYAPVLODFRSLNDSTNRTKKAHNSKSGEENLEGLGNQTKOYIEKACTRTISPT 1320  
DB 1261 GAYAPVLODFRSLNDSTNRTKKAHNSKSGEENLEGLGNQTKOYIEKACTRTISPT 1320  
QY 1321 SQONFVYORSKRALKOFRLPLEETELEKRIIVDDTSTOKSKMKHLTPSTLIOIDYNEKE 1380  
DB 1321 SQONFVYORSKRALKOFRLPLEETELEKRIIVDDTSTOKSKMKHLTPSTLIOIDYNEKE 1380  
QY 1381 KGATLOSPLSDCLTSHSITPOANSPLPIKAYSFPSTIRPIYLRVLPONSSHLPLAASY 1440  
DB 1381 KGATLOSPLSDCLTSHSITPOANSPLPIKAYSFPSTIRPIYLRVLPONSSHLPLAASY 1440  
QY 1441 RKDSGVQESSHFLGQAKKNNLSAILLTLEMTGDORVSGLSTANVSITYKKEVNTVLP 1500  
DB 1441 RKDSGVQESSHFLGQAKKNNLSAILLTLEMTGDORVSGLSTANVSITYKKEVNTVLP 1500  
QY 1501 KPDLPKTSQVLELLEPKVHIYOKDLFPEITSNGSPGLDLYEGSLLAGTTEGAIKWNAANRP 1560  
DB 1501 KPDLPKTSQVLELLEPKVHIYOKDLFPEITSNGSPGLDLYEGSLLAGTTEGAIKWNAANRP 1560  
QY 1561 GKVPFLVATTESSAKTPKLDLPLAMNHNQGIPIPEEKMSQEKSPKTAFFKKDITLSTL 1620  
DB 1561 GKVPFLVATTESSAKTPKLDLPLAMNHNQGIPIPEEKMSQEKSPKTAFFKKDITLSTL 1620  
QY 1621 NACESNHAIAINEGQNPETIEVTWANOFTERTLCSQNPVLRKHOREIRTTLOSDOE 1680  
DB 1621 NACESNHAIAIAINEGQNPETIEVTWANOFTERTLCSQNPVLRKHOREIRTTLOSDOE 1680  
QY 1681 IDYDDTISYEMKKEPFDIYDEDDENQSPRSOKTTRYFAANVERLMTYGGSSPHYLNR 1740  
DB 1681 IDYDDTISYEMKKEPFDIYDEDDENQSPRSOKTTRYFAANVERLMTYGGSSPHYLNR 1740





301 ROASLETSPELELLAQTLIDLGOFILFCHHSHOHGMEAYVYKDSCEEPPEOLRMNNE 360  
361 EAEYDODLTDSEMDVYRFDONSPSFOIRSVAKKHPTWYHYIAAEEBMDAPLYLA 420  
361 EAEYDODLTDSEMDVYRFDONSPSFOIRSVAKKHPTWYHYIAAEEBMDAPLYLA 420  
421 PDORSYKSOYLANGPORIGRKYKKVREMAVYDETFTKREAIQHESGILGPILYGEVDTL 480  
421 PDORSYKSOYLANGPORIGRKYKKVREMAVYDETFTKREAIQHESGILGPILYGEVDTL 480  
481 LIIFKNASRPYNYPHGITDVRPLYSRPLPKGYKHLKDEPLIPGEIFEYKWTYVEDGP 540  
481 LIIFKNASRPYNYPHGITDVRPLYSRPLPKGYKHLKDEPLIPGEIFEYKWTYVEDGP 540  
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541 TKSDPRLCTRYSSFYVNMERDLASGLIGPLLCYKESVDQKQNMDSKRNVIYFSVDE 600  
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601 NRSWYLTENIORPLPMPAGVQLEDEFOASNIMHSINGYFDSILOSLVCLHEVAWYLLS 660  
661 IGAOTDPLSVFESGTYFFKHKMYEDTTLTPFPSEYVMSMENPGMLTICGHSNDFNRNG 720  
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721 MTALLKYSQCDKNTGUYEDYEDISAVLLSKNNAIEPRFSQNSRHPSTROKQFNATTI 780  
781 PENDIEKTDWFA - RTMPKIQNVSSDLMMLKQSPTPHGLSLDLOAKETSSDPS 840  
781 PENDIEKTDWFA - RTMPKIQNVSSDLMMLKQSPTPHGLSLDLOAKETSSDPS 840  
841 PGALIDNNNSLEMTNHRPQLHHSQDMVTPESGQLRLNKLKGTATLKLKDFKVSST 900  
841 PGALIDNNNSLEMTNHRPQLHHSQDMVTPESGQLRLNKLKGTATLKLKDFKVSST 900  
901 SNNLITPISPDNLAACTDNTSSIGPSPMYADSLDTTLFGKSSPLFEESGSPISLEE 960  
901 SNNLITPISPDNLAACTDNTSSIGPSPMYADSLDTTLFGKSSPLFEESGSPISLEE 960  
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1021 KTSNNSATNKRKTHIDPSSLIIENSPVQNTLESDTEFKKVTPLIHDRMLMKNTALRL 1080  
1081 NHMSNKTTSKKNMDEMYOQKKEGPIPPDAQNPDMSFFKMLFLPESARWIOPTHGKNSLNSG 1140  
1081 NHMSNKTTSKKNMDEMYOQKKEGPIPPDAQNPDMSFFKMLFLPESARWIOPTHGKNSLNSG 1140  
1141 OGSPSKOLVSLGPEKSEYEGONFLSEKNKYVYGKEFTKDVGLKEMVFPSSRMLFTLNIDN 1200  
1141 OGSPSKOLVSLGPEKSEYEGONFLSEKNKYVYGKEFTKDVGLKEMVFPSSRMLFTLNIDN 1200  
1201 LHENNTNHOEKKIOEIELEKTELIOENVVLPQIHTVTGKNFMKNLFLSTRQNVESGYD 1260  
1201 LHENNTNHOEKKIOEIELEKTELIOENVVLPQIHTVTGKNFMKNLFLSTRQNVESGYD 1260  
1261 GAYAVIADPFRSLNDSTNRTKKHTAHFSGKEEENLEGIGNOTKOIYEVYACTRTISNT 1320  
1261 GAYAVIADPFRSLNDSTNRTKKHTAHFSGKEEENLEGIGNOTKOIYEVYACTRTISNT 1320  
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1320 SOONFVTOQRSKRALKOFRLPLEETLEKRIIVDTSTQWSKNNKHLTPSTLOIDYNEKE 1380  
1381 KGAITQSPISDCLTRHSNIPQANRSPPLIAKVSPPSIRPYTLRYLFDONSSHLPAASY 1440  
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1380 KGAITQSPISDCLTRHSNIPQANRSPPLIAKVSPPSIRPYTLRYLFDONSSHLPAASY 1439  
1441 RKKDSVOESSHFLQAGAKKNNLSIALTLTLEMTGDQREVSGLSATNSVYKKVENTYLP 1500  
1440 RKKDSVOESSHFLQAGAKKNNLSIALTLTLEMTGDQREVSGLSATNSVYKKVENTYLP 1499  
1501 KPDLKTSKGKVELPKYHIYQKRLPFTESNCSPGHIDLVGSLIQTGEGAIKMNENAPR 1560  
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1561 GRVPELRVATESAKTESKLLDLPLADNHYGQIAPKEBMSQEKSPKTAFFKKDTIISL 1620  
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1621 NCESNHAIAINEGOKKPELEYTMAKQRTRELCSQNPPLKRRHQREITRTLOSDOE 1680  
1620 NCESNHAIAINEGOKKPELEYTMAKQRTRELCSQNPPLKRRHQREITRTLOSDOE 1679  
1681 IDYDPTISVEKKEDPDIYDEENOSPSFOKTRHYIAAVERLMDYGSSPHYLRNR 1740  
1680 IDYDPTISVEKKEDPDIYDEENOSPSFOKTRHYIAAVERLMDYGSSPHYLRNR 1739  
1741 AOSGSVPQKKVYFOEFTDGSFTQPLYRGELEHGLGPYIRAEVEDNIMVFRNOASR 1800  
1740 AOSGSVPQKKVYFOEFTDGSFTQPLYRGELEHGLGPYIRAEVEDNIMVFRNOASR 1799  
1801 PVSFYSLSIYEBDQROGAEBRKNFYKPNETKTYTWKYQHHMAPTKDEPCKMAAFESV 1860  
1800 PVSFYSLSIYEBDQROGAEBRKNFYKPNETKTYTWKYQHHMAPTKDEPCKMAAFESV 1859  
1861 DLEKDVHSLIGPLLYCHTNTLPANRQVYVQOEALFTTIFEDTKSMYTEMENENCA 1920  
1860 DLEKDVHSLIGPLLYCHTNTLPANRQVYVQOEALFTTIFEDTKSMYTEMENENCA 1919  
1921 PCNIOMEDTEKENTRERHAINGTIMDTLPGLYMAQDOIRMYLLSKMSNNHSHHSFSGH 1980  
1920 PCNIOMEDTEKENTRERHAINGTIMDTLPGLYMAQDOIRMYLLSKMSNNHSHHSFSGH 1979  
1981 VFTVRKKEEYKALYNYLPGVETVEMLPSKAGIWRVCLIGEHLHAGMSTLFLVYSNKC 2040  
1980 VFTVRKKEEYKALYNYLPGVETVEMLPSKAGIWRVCLIGEHLHAGMSTLFLVYSNKC 2039  
2041 QTPFLGMASSHINDPOTYASQYQGMAPKLABLHYSGSTINASTKEPSWIKVDLAPMII 2100  
2040 QTPFLGMASSHINDPOTYASQYQGMAPKLABLHYSGSTINASTKEPSWIKVDLAPMII 2099  
2101 HGIKTQGARQKFSLSLYISQFTIMYSLDGKKMOTYRGNSTGTLWVFGNVDSGSIKHNIFN 2160  
2100 HGIKTQGARQKFSLSLYISQFTIMYSLDGKKMOTYRGNSTGTLWVFGNVDSGSIKHNIFN 2159  
2161 PPIIARYTILHPTHTSIRSTLRMELMGCDLNSGMPDGESKATSDAQITASSYFTNMFA 2220  
2160 PPIIARYTILHPTHTSIRSTLRMELMGCDLNSGMPDGESKATSDAQITASSYFTNMFA 2219  
2221 TWSPSKARILHLOGRSNANRPVQNNPKEMLOVDFOKTMKVYGVTTQGYKSLTJSMYKEFL 2280  
2220 TWSPSKARILHLOGRSNANRPVQNNPKEMLOVDFOKTMKVYGVTTQGYKSLTJSMYKEFL 2279  
2281 ISSSOGHGWTLFFRQNGVYKVEQGNDSFPPVYNSILDEPLLRITLRHPQSWHQAIALRN 2340  
2280 ISSSOGHGWTLFFRQNGVYKVEQGNDSFPPVYNSILDEPLLRITLRHPQSWHQAIALRN 2339  
2341 EYLGECAODLY 2351  
2340 EYLGECAODLY 2350

RESULT 87  
AAM11443  
ID AAM11443 standard; Protein; 2349 AA.  
XX AC AAM11443;  
XX

DT	20-NOV-1997	(first entry)
XX	Active Factor VIII:C analogue residue 1642, 1643 deletion.	
DE		
XX	Factor VIII:C; analogue: glycoprotein; blood coagulation cascade; fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis; plasma protease; thrombin; immunogen; antibody; haemophilia; therapy; proteolytic cleavage.	
KW		
KM		
XX	Homo sapiens.	
OS	Synthetic.	
XX		
FT	Key	
FT	Location/Qualifiers	
FT	Peptide	
FT	1..19	
FT	/note= "signal peptide"	
FT	Protein	
FT	20..2349	
FT	/note= "mature Factor VIII:C"	
FT	Region	
FT	20..1665	
FT	/note= "heavy chain fragment"	
FT	Misc-difference	
FT	1660..1661	
FT	/note= "site of 2 residue deletion"	
FT	Region	
FT	1666..2348	
FT	/note= "light chain fragment"	
FT	Domain	
FT	760..1665	
FT	/note= "B domain"	
XX		
XX	MO9703195-A1.	
PN		
XX	30-JAN-1997.	
PD		
XX		
XX	09-JUL-1996; 96WO-US11444.	
PE		
XX		
PR	11-JUL-1995; 95US-0001025.	
PA		
XX	(CHIR ) CHIRON CORP.	
PI		
XX	Cohen FE, Hung DT, Innis M;	
DR	WPI; 1997-119050/11.	
XX		
PT	Factor VIII:C analog modified adjacent to a non-activating Arg	
PT	residue - used in the treatment of haemophiliacs, by improvement of	
PT	haemostasis	
XX		
PS	Claim 32; Page -: 90pp; English.	
XX		
CC	AAW1330-W1472 represent active Factor VIII:C analogues of the	
CC	invention. These sequences were created by mutating the wild type Factor	
CC	VIII:C coding sequence (see AAT51357) using mutagenic primers. The	
CC	analogues comprise a native Factor VIII:C polypeptide modified at a site	
CC	adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg	
CC	dipeptide is created. Factor VIII:C is a large glycoprotein that	
CC	participates in the blood coagulation cascade that ultimately converts	
CC	soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A	
CC	deficiency in Factor VIII:C is responsible for haemophilia A, which is an	
CC	X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is	
CC	activated by plasma proteases, such as thrombin. During activation the	
CC	mature polypeptide is cleaved to generate heavy and light chain fragments	
CC	that are further cleaved. Complexes of two or more of the analogues,	
CC	nucleic acids and vectors encoding them may be used alone or in	
CC	conjunction with each other, for the prevention or treatment of active	
CC	Factor VIII:C deficiency in a mammal. The analogues may be used as	
CC	immunogens to raise antibodies, and in the treatment of haemophiliacs, by	
CC	improvement of haemostasis. The analogues are resistant to proteolytic	
CC	cleavage and display increased plasma half-life. They may be administered	
CC	at lower dosages and by different modes of administration.	
XX		
SQ	Sequence 2349 AA:	
Query Match	99.8%; Score 12399; DB 18; Length 2349;	
Best Local Similarity	99.9%; Pred. No. 0;	
Matches 2349; Conservative	0; Mismatches 0; Indels 2; Gaps 1;	

QY	1	MOIELSTCFELCLRECFESATRRYYIGAVEISMDYMOISDLGELPYDARPPRPVPSFPFN	60
DB	1	MOIELSTCFELCLRECFESATRRYYIGAVEISMDYMOISDLGELPYDARPPRPVPSFPFN	60
QY	61	TSVYVKKTLFVEETDHLFNTAKPRPMWMLGPTLOAEVDYVITLKKMASSPVSIAV	120
DB	61	TSVYVKKTLFVEETDHLFNTAKPRPMWMLGPTLOAEVDYVITLKKMASSPVSIAV	120
QY	121	GVSTWKASGEAYDDOTSOKEKEDKVPEGSHYVQVLKENGPAADPLCLTYSLSH	180
DB	121	GVSTWKASGEAYDDOTSOKEKEDKVPEGSHYVQVLKENGPAADPLCLTYSLSH	180
QY	181	VDLVKDLNSGLIGALLVCREGSLAKEKOTLHKFTLLFAVFDGKSMHSETKNSLMORD	240
DB	181	VDLVKDLNSGLIGALLVCREGSLAKEKOTLHKFTLLFAVFDGKSMHSETKNSLMORD	240
QY	241	AASARAMPKHTVNGVYNSLPGILGCHRSKYVHWVIGMGTPEVHSITLBSHTFLVRNH	300
DB	241	AASARAMPKHTVNGVYNSLPGILGCHRSKYVHWVIGMGTPEVHSITLBSHTFLVRNH	300
QY	301	ROASHBLSPTLFTLAOTLMDLGOFLFCCHISSHQHDGMEAYVKVDSCEEPQLMKKNE	360
DB	301	ROASHBLSPTLFTLAOTLMDLGOFLFCCHISSHQHDGMEAYVKVDSCEEPQLMKKNE	360
QY	361	EAEYDDDLTDSMDYVRDDDNSSPFIQISYAKKPKTWHTYIAAEEEDMDYAPLYA	420
DB	361	EAEYDDDLTDSMDYVRDDDNSSPFIQISYAKKPKTWHTYIAAEEEDMDYAPLYA	420
QY	421	PDDRSYKSOYLNNGPORIGRKYKRVFAYVDEFKTRREALIQHESGILGPLLGEVGDTL	480
DB	421	PDDRSYKSOYLNNGPORIGRKYKRVFAYVDEFKTRREALIQHESGILGPLLGEVGDTL	480
QY	481	LIIFKNASRPYNIYHGHTDYRPLYSRRLKGVKHLKDPILPGSIFKPKTWVEEGP	540
DB	481	LIIFKNASRPYNIYHGHTDYRPLYSRRLKGVKHLKDPILPGSIFKPKTWVEEGP	540
QY	541	TKSDPCLTRYSSFFVNMERDLASGLIGPLLCYKESVDGRGNOIMSDKRNVIIFYEDE	600
DB	541	TKSDPCLTRYSSFFVNMERDLASGLIGPLLCYKESVDGRGNOIMSDKRNVIIFYEDE	600
QY	601	NRSWYLTENIORPLPAPAGVOLEDEPQASIMHSINGVYFOSLOLSCVLEHVAWYTLIS	660
DB	601	NRSWYLTENIORPLPAPAGVOLEDEPQASIMHSINGVYFOSLOLSCVLEHVAWYTLIS	660
QY	661	IGAOTDFLVFESGYFKHKVYEDTLTLFPFSGETVFSMENPGMLIAGCHNSDFRNG	720
DB	661	IGAOTDFLVFESGYFKHKVYEDTLTLFPFSGETVFSMENPGMLIAGCHNSDFRNG	720
QY	721	MTALLKVSQCDKMTGQDYEDSYEDISAVILSKNNAIEPNSFSONSHRSTOKOPNAATTI	780
DB	721	MTALLKVSQCDKMTGQDYEDSYEDISAVILSKNNAIEPNSFSONSHRSTOKOPNAATTI	780
QY	781	PENDIEKTPWFAHRTPMKIONVSSSDDLMLRQSTPFGLSLDQEAKEYTFSDPS	840
DB	781	PENDIEKTPWFAHRTPMKIONVSSSDDLMLRQSTPFGLSLDQEAKEYTFSDPS	840
QY	841	PGALDSNNSLSEKTHFRPOLHHSQMYFTSPSGLOLRUNKLGTAAAEIKKLDFKXST	900
DB	841	PGALDSNNSLSEKTHFRPOLHHSQMYFTSPSGLOLRUNKLGTAAAEIKKLDFKXST	900
QY	901	SNNLSTITSNDLAACTDNTSSLCRPPSPVHYDSQDITLFLFKKSSPLTESGGLSSEE	960
DB	901	SNNLSTITSNDLAACTDNTSSLCRPPSPVHYDSQDITLFLFKKSSPLTESGGLSSEE	960
QY	961	NDSKLLSEGLANNSOESSMGKNVSSSTSGRLFGKRAHAPALLTVDNALFPVYSILKTN	1020
DB	961	NDSKLLSEGLANNSOESSMGKNVSSSTSGRLFGKRAHAPALLTVDNALFPVYSILKTN	1020
QY	1021	KTSSNSATNRKTHIDGPELLIENSFWONITLESDEFEKKTYPPLTHRBMILMDKNAATLRL	1080
DB	1021	KTSSNSATNRKTHIDGPELLIENSFWONITLESDEFEKKTYPPLTHRBMILMDKNAATLRL	1080
QY	1081	NHMSNKTTSKKNMEVQOKKEGPIPDQAQNPDKSFFKMLFLPESARWIOIRHGNLSLNG	1140

1081 NHMSKNTSSKNMDEMVOQKKEGPIPPDQNDMSEFFKMLFLPESARVIORTGKKSLSNG 1140  
1141 QGSPKQVLSPGPKSVESQNFLESEKKNVYVKGEEFTKDVGLKEMVFPSSRNLFJTNLDN 1200  
1141 QGSPKQVLSPGPKSVESQNFLESEKKNVYVKGEEFTKDVGLKEMVFPSSRNLFJTNLDN 1200  
1201 LHENNTNHOEKKIOEETIEKKEFTLIOENVVLPQIHTVTGTRKFKNLFJLSTQONESGYD 1260  
1201 LHENNTNHOEKKIOEETIEKKEFTLIOENVVLPQIHTVTGTRKFKNLFJLSTQONESGYD 1260  
1261 GATAPVLODRRLNDSTNRTKKTAAHFSKKEEENLGLGNQTKQVEYXACTRIISPT 1320  
1261 GATAPVLODRRLNDSTNRTKKTAAHFSKKEEENLGLGNQTKQVEYXACTRIISPT 1320  
1321 SQONFTQSRKALQOFRLPLEETELEKRIIVDDTSTQMSKNNKHLPTLTQIDYNEKE 1380  
1321 SQONFTQSRKALQOFRLPLEETELEKRIIVDDTSTQMSKNNKHLPTLTQIDYNEKE 1380  
1381 KGATQSPSLDCLTRSHSTPOANRSPPLPAKVSPSPTRPIYLTRVLPQDNSSHLPAASY 1440  
1381 KGATQSPSLDCLTRSHSTPOANRSPPLPAKVSPSPTRPIYLTRVLPQDNSSHLPAASY 1440  
1441 RKDSGVQESSHFLQGAKKNNLSLAILEMTGQDREVSIGTSATNSVYTKKVENTVLP 1500  
1441 RKDSGVQESSHFLQGAKKNNLSLAILEMTGQDREVSIGTSATNSVYTKKVENTVLP 1500  
1501 KPDLPKTSQKVELLPKHVIYOKDLPTTESNGSPGHLDIVESLLOGTGAIKWEANRP 1560  
1501 KPDLPKTSQKVELLPKHVIYOKDLPTTESNGSPGHLDIVESLLOGTGAIKWEANRP 1560  
1501 KPDLPKTSQKVELLPKHVIYOKDLPTTESNGSPGHLDIVESLLOGTGAIKWEANRP 1560  
1561 GKVPFLRVATESSAKTPSKLLDPLAMDNHYGTQIPKEBMSQESPKTAFFKKDTIISL 1620  
1561 GKVPFLRVATESSAKTPSKLLDPLAMDNHYGTQIPKEBMSQESPKTAFFKKDTIISL 1620  
1621 NACEGNHAIIAINNGOKKPEIEVTNAKOGTRPRLCSQNPVLRKHQREITRTLLQDOEE 1680  
1621 NACEGNHAIIAINNGOKKPEIEVTNAKOGTRPRLCSQNPVLRKHQREITRTLLQDOEE 1680  
1681 IDYDTISVEKKKDDPIYDEBENOSPRFOKKTTHFTIAVERLMDYGMSSPHVLRNR 1740  
1681 IDYDTISVEKKKDDPIYDEBENOSPRFOKKTTHFTIAVERLMDYGMSSPHVLRNR 1740  
1739 AQSQSVPOFKKVVQFQETDGSFTQPIRYGELNEHLGLGPYRAVEDNIMVTFRNOASR 1800  
1739 AQSQSVPOFKKVVQFQETDGSFTQPIRYGELNEHLGLGPYRAVEDNIMVTFRNOASR 1800  
1801 PYSFYSLSIYEEOQOGAEPKRNFKPMEKTYRMYKQOHMAPTKDEPCKAMAFESPV 1860  
1801 PYSFYSLSIYEEOQOGAEPKRNFKPMEKTYRMYKQOHMAPTKDEPCKAMAFESPV 1860  
1861 DLEKDVHSLIGLPLVCHTNTLPAHGRQVTVQEFALFTTIFDETKSWYTEMERNCRA 1920  
1861 DLEKDVHSLIGLPLVCHTNTLPAHGRQVTVQEFALFTTIFDETKSWYTEMERNCRA 1920  
1919 PCNIQMEDPTFKENYRHHAINGYIMDTLPGLVADODRIRVYLLSMGSNNIHSHFSGH 1980  
1919 PCNIQMEDPTFKENYRHHAINGYIMDTLPGLVADODRIRVYLLSMGSNNIHSHFSGH 1980  
1979 VFTVVRKKEEYKMAIYNLYPGVFETVEMLPKAGIRVCECLLGEHLAGMSTFLVYSNCC 2038  
2041 QTPGLMASGHTRDFOITASGOYGOWAPKLARIHYSGSINAMSTKEPSPWIKVLLAPMTI 2100  
2041 QTPGLMASGHTRDFOITASGOYGOWAPKLARIHYSGSINAMSTKEPSPWIKVLLAPMTI 2100  
2098 HGKTQGAOKFSSLYISQFTIMYSLDGKKWQTYRGNSTGTIMVFGNVDSGSIKHNIFN 2158  
2098 HGKTQGAOKFSSLYISQFTIMYSLDGKKWQTYRGNSTGTIMVFGNVDSGSIKHNIFN 2158  
2161 PPIIARYTRLHPTHTYSTRSLRMEIMGCDLNSCSPMLMESKAIISDOITASSYFTNMFA 2220  
2161 PPIIARYTRLHPTHTYSTRSLRMEIMGCDLNSCSPMLMESKAIISDOITASSYFTNMFA 2220

2159 PPIIARYTRLHPTHTYSTRSLRMEIMGCDLNSCSPMLMESKAIISDOITASSYFTNMFA 2218  
2221 TWSPSKARLHLOGSNAMARPOVNNPKEMLOVPOFTMKVCTTQGVKSLLTSMYKEFL 2280  
2219 TWSPSKARLHLOGSNAMARPOVNNPKEMLOVPOFTMKVCTTQGVKSLLTSMYKEFL 2278  
2281 ISSSQDQHWMTLFPQNGKVKVFGQNDSTFPVYNSLDPPLTRILRIHPQSWHQIALRM 2340  
2279 ISSSQDQHWMTLFPQNGKVKVFGQNDSTFPVYNSLDPPLTRILRIHPQSWHQIALRM 2338  
2341 EYLCEADPLY 2351  
2339 EYLCEADPLY 2349  
RESULT 88  
AAW11472  
ID AAW11472 standard; Protein; 2351 AA.  
AC AAW11472;  
XX 21-NOV-1997 (first entry)  
XX Active Factor VIII:C analogue, R336P, R1719P, R1721E.  
DE Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;  
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KW plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;  
XX proteolytic cleavage.  
XX Homo sapiens.  
OS Synthetic.  
XX  
XX Key Location/Qualifiers  
FH 1..19  
FT /note= "signal peptide"  
FT Protein 20..2350  
FT /note= "mature Factor VIII:C"  
FT Region 20..1667  
FT /note= "heavy chain fragment"  
FT Modified-site 355  
FT /label= R336P  
FT Domain 759..1667  
FT /note= "B domain"  
FT Region 1668..2349  
FT /note= "light chain fragment"  
FT Modified-site 1738  
FT /label= R1719P  
FT Modified-site 1740  
FT /label= R1721E  
XX W09703195-A1.  
XX 30-JAN-1997.  
XX PD  
XX 09-JUL-1996; 96MO-US11444.  
XX PR 11-JUL-1995; 95US-0001025.  
XX (CHIR ) CHIRON CORP.  
XX Cohen FE, Hung DT, Innis M;  
XX  
XX WPI; 1997-119050/11.  
XX  
XX Factor VIII:C analog modified adjacent to a non-activating Arg  
XX residue used in the treatment of haemophiliacs, by improvement of  
XX haemostasis  
XX  
XX Claim 40; Page -: 90pp; English.  
CC AAW11330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor





Qy 421 PDDRSYKSOYLNNNGPQIRGRKTKKVRFAAYTDETFKTREAIQIHESGILGPIILGYEGDTL 480  
|||||  
Db 421 PDDRSYKSOYLNNNGPQIRGRKTKKVRFAAYTDETFKTREAIQIHESGILGPIILGYEGDTL 480  
Qy 481 LIIFKNOASRPYNYTPHGIITDVRLYSHRLPKYKHLKDFPIILGEIEFKKVTYVEDGP 540  
|||||  
Db 481 LIIFKNOASRPYNYTPHGIITDVRLYSHRLPKYKHLKDFPIILGEIEFKKVTYVEDGP 540  
Qy 541 TKSDPRCLTRYSSFFVNMERDLASGLIGPLILCYKESVDQGNQIIMSDKRNVIJFSVDE 600  
|||||  
Db 541 TKSDPRCLTRYSSFFVNMERDLASGLIGPLILCYKESVDQGNQIIMSDKRNVIJFSVDE 600  
Qy 601 NRSWTJENTIORFLPNPAGVQLEDEPFOASNIHMSINGYVDSLOLSTVCLHEVAYWILS 660  
|||||  
Db 601 NRSWTJENTIORFLPNPAGVQLEDEPFOASNIHMSINGYVDSLOLSTVCLHEVAYWILS 660  
Qy 661 IGAQOTDFLSVFFSGYTFKKHMYEDTLTLFPFSGEIVFMSMENPGLMILGCHNSDFNRNG 720  
|||||  
Db 661 IGAQOTDFLSVFFSGYTFKKHMYEDTLTLFPFSGEIVFMSMENPGLMILGCHNSDFNRNG 720  
Qy 721 MTALLKVSQDKNTGVDYEDSYEDISAYLLSKNNAIEPRFSQNSRHPSTROKOPNATTI 780  
|||||  
Db 721 MTALLKVSQDKNTGVDYEDSYEDISAYLLSKNNAIEPRFSQNSRHPSTROKOPNATTI 780  
Qy 781 PENDIKTDPPFAHRRTPMKTIONVSSSDMLILKQSPTRHGLSLSDLOAKYETFSDDPS 840  
|||||  
Db 781 PENDIKTDPPFAHRRTPMKTIONVSSSDMLILKQSPTRHGLSLSDLOAKYETFSDDPS 840  
Qy 841 PGALIDSNNLSSEWTHFRPOLHSGDMVTPPSGLOLRINEKLGTTAAETELKLFKVSST 900  
|||||  
Db 841 PGALIDSNNLSSEWTHFRPOLHSGDMVTPPSGLOLRINEKLGTTAAETELKLFKVSST 900  
Qy 901 SNNLISTIPSDNLAAGDNTSSLAGPPSPMVHYDSQDLDTLFGKSSPLTESGCPILSSEE 960  
|||||  
Db 901 SNNLISTIPSDNLAAGDNTSSLAGPPSPMVHYDSQDLDTLFGKSSPLTESGCPILSSEE 960  
Qy 961 NNDKSLLESGLANSQESGKXVSTESBGRLFKRAHAGALLTKNALFKYISLKTIN 1020  
|||||  
Db 961 NNDKSLLESGLANSQESGKXVSTESBGRLFKRAHAGALLTKNALFKYISLKTIN 1020  
Qy 1021 KTSNNSATNRKTHIDGSPSLIENSPPVQNTLESDETEFKKVTPLIHDRMLMDKNATLRL 1080  
|||||  
Db 1021 KTSNNSATNRKTHIDGSPSLIENSPPVQNTLESDETEFKKVTPLIHDRMLMDKNATLRL 1080  
Qy 1081 NMSNKTSSKNNMVOQKKEGPIPPDAONPDMSFEFKMLFLPPSARWIORTHGKXSLNSG 1140  
|||||  
Db 1081 NMSNKTSSKNNMVOQKKEGPIPPDAONPDMSFEFKMLFLPPSARWIORTHGKXSLNSG 1140  
Qy 1141 OGSPKOLVSLGPKSVYEGONFLSEKKNVYVGKEFTKDVGLKEWVFPSSRNLFJTLNDN 1200  
|||||  
Db 1141 OGSPKOLVSLGPKSVYEGONFLSEKKNVYVGKEFTKDVGLKEWVFPSSRNLFJTLNDN 1200  
Qy 1201 LHENNTNHQEKKIOEIEKEKETLIQBNVVLPOIITVGTGKNFKNLFLJLSTRONEGSYD 1260  
|||||  
Db 1201 LHENNTNHQEKKIOEIEKEKETLIQBNVVLPOIITVGTGKNFKNLFLJLSTRONEGSYD 1260  
Qy 1261 GAYAVLODFRSLDSDNRTKKTHTAFSKGKEEENLEGLNOKOIVEKYACTPRLISNT 1320  
|||||  
Db 1261 GAYAVLODFRSLDSDNRTKKTHTAFSKGKEEENLEGLNOKOIVEKYACTPRLISNT 1320  
Qy 1321 SOONFVORSKRALKQRLPLEBTELEKRIIVDTSTQMSKNNKHLJPSTLQIDYNEKE 1380  
|||||  
Db 1321 SOONFVORSKRALKQRLPLEBTELEKRIIVDTSTQMSKNNKHLJPSTLQIDYNEKE 1380  
Qy 1381 KGAIQSPUSDCLTRSHSIFPOANRSPPLIAKVSSFPPIRPIYLRVLFQDNSSHLPAASY 1440  
|||||  
Db 1381 KGAIQSPUSDCLTRSHSIFPOANRSPPLIAKVSSFPPIRPIYLRVLFQDNSSHLPAASY 1440  
Qy 1441 RKKDSGVOESSHPLQGGAKKNNLSLAILTLEMTGQOREVGSLSGTSANSTYKAVNTYLP 1500  
|||||  
Db 1441 RKKDSGVOESSHPLQGGAKKNNLSLAILTLEMTGQOREVGSLSGTSANSTYKAVNTYLP 1500  
Qy 1439 RKKDSGVOESSHPLQGGAKKNNLSLAILTLEMTGQOREVGSLSGTSANSTYKAVNTYLP 1498  
|||||

Qy 1501 KPDLPTSGKVELLPRKHVITOKDLPFETNSGSPGHLDLVEGSLQGTGCAIKNNEANRP 1560  
|||||  
Db 1499 KPDLPTSGKVELLPRKHVITOKDLPFETNSGSPGHLDLVEGSLQGTGCAIKNNEANRP 1558  
Qy 1561 GVPFLRLVATSSAKTPRSKILDLPLAMDNYGTQIPKREEMSOQSPKTAKKKDTLISL 1620  
|||||  
Db 1559 GVPFLRLVATSSAKTPRSKILDLPLAMDNYGTQIPKREEMSOQSPKTAKKKDTLISL 1618  
Qy 1621 NACESNHAIAINQGNKPEIEVTAKOGRTERRCSQNPVLRKHQREITRTTLQSDQEE 1680  
|||||  
Db 1619 NACESNHAIAINQGNKPEIEVTAKOGRTERRCSQNPVLRKHQREITRTTLQSDQEE 1678  
Qy 1681 IDYDITISVEKKKEDPIDDEBNOSPPSKRPHFTAAVRRLMDXNSSPHVLR 1740  
|||||  
Db 1679 IDYDITISVEKKKEDPIDDEBNOSPPSKRPHFTAAVRRLMDXNSSPHVLR 1738  
Qy 1741 AQSQSVPOFKKVVFOEFTDGSFTOPLRYGELNEHILGLGYIRAEVEDINWTERNOASR 1800  
|||||  
Db 1739 AQSQSVPOFKKVVFOEFTDGSFTOPLRYGELNEHILGLGYIRAEVEDINWTERNOASR 1798  
Qy 1801 PYSFYSLSIYEEDROGAEPKRNFKPNETKTYFMKVQHNNAPTKDEBDCKAMAYESDV 1860  
|||||  
Db 1799 PYSFYSLSIYEEDROGAEPKRNFKPNETKTYFMKVQHNNAPTKDEBDCKAMAYESDV 1858  
Qy 1861 DLEKDVHSLIGRLYCHHTYTLNPAHGOVTVQBFALFTIPDETSMVPEPMNRNCR 1920  
|||||  
Db 1859 DLEKDVHSLIGRLYCHHTYTLNPAHGOVTVQBFALFTIPDETSMVPEPMNRNCR 1918  
Qy 1921 PCNIQMEDPTEKENYRPHALNGYIMDTLPGLVMAODRIRMYLLSGNSNENIHSIHESGH 1980  
|||||  
Db 1919 PCNIQMEDPTEKENYRPHALNGYIMDTLPGLVMAODRIRMYLLSGNSNENIHSIHESGH 1978  
Qy 1981 VFTYARKKEEYKMALYNLYPGVEVEYMLPSKAGIMRVECLIGELHLAGNSTLFLVYSNK 2040  
|||||  
Db 1979 VFTYARKKEEYKMALYNLYPGVEVEYMLPSKAGIMRVECLIGELHLAGNSTLFLVYSNK 2038  
Qy 2041 QTPFLMASGHTIRDOQTASQOIGONAPKTLARLHSSGINSINASTKEPFSIKVDLAPRII 2100  
|||||  
Db 2039 QTPFLMASGHTIRDOQTASQOIGONAPKTLARLHSSGINSINASTKEPFSIKVDLAPRII 2098  
Qy 2101 HGKITOGAROKFSSLYISOFIIMYSLDKKKQTYRGNSTGLTWVFGVNDSSGIKHNTFN 2160  
|||||  
Db 2099 HGKITOGAROKFSSLYISOFIIMYSLDKKKQTYRGNSTGLTWVFGVNDSSGIKHNTFN 2158  
Qy 2161 PPIIARVRLHPHTYSIRSLHMEIAGCDLNSGMPRLGMSKASISAOITTASSTYTNFA 2220  
|||||  
Db 2159 PPIIARVRLHPHTYSIRSLHMEIAGCDLNSGMPRLGMSKASISAOITTASSTYTNFA 2218  
Qy 2221 TWSPSKARLHLOGRSNAMPQVNNPREMLQVDFOKTYKVTGVTGCVKSLTSMYVEFL 2280  
|||||  
Db 2219 TWSPSKARLHLOGRSNAMPQVNNPREMLQVDFOKTYKVTGVTGCVKSLTSMYVEFL 2278  
Qy 2281 ISSSODGHQMTLFPQNGKXVFEQGNDSFTPVVNSLDPPLLTRYLRIHPQSVHQAIALRM 2340  
|||||  
Db 2279 ISSSODGHQMTLFPQNGKXVFEQGNDSFTPVVNSLDPPLLTRYLRIHPQSVHQAIALRM 2338  
Qy 2341 EYLGEAQDLY 2351  
|||||  
Db 2339 EYLGEAQDLY 2349  
|||||

RESULT 90  
AAM1373  
ID AAM1373 standard; Protein; 2349 AA.  
XX  
AC AAM1373;  
XX  
XX 18-NOV-1997 (first entry)  
DT  
XX  
DE Active Factor VIII:C analogue residue 334, 335 deletion.  
XX  
KW Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;  
fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;

KM plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;  
KM proteolytic cleavage.  
XX Homo sapiens.  
OS Synthetic.  
XX  
FH Key Location/Qualifiers  
FT Peptide 1..19  
FT /note= "signal peptide"  
FT Protein 20..2349  
FT /note= "mature Factor VIII:C"  
FT Region 20..1665  
FT /note= "heavy chain fragment"  
FT Misc-difference 352..353  
FT /note= "site of 2 residue deletion"  
FT Region 1666..2348  
FT /note= "light chain fragment"  
FT Domain 758..1665  
FT /note= "B domain"  
XX  
XX W09703195-A1.  
XX  
XX 30-JAN-1997.  
XX  
XX 09-JUL-1996; 96WO-051144.  
XX  
XX 11-JUL-1995; 95US-0001025.  
XX  
XX (CHIR ) CHIRON CORP.  
XX  
XX Cohen FE, Hung DT, Innis M;  
XX WPI; 1997-119050/11.  
XX  
XX Factor VIII:C analog modified adjacent to a non-activating Arg  
XX residue - used in the treatment of haemophilias, by improvement of  
XX haemostasis  
XX  
XX Claim 17: Page -: 90pp: English.  
XX  
XX AAM11330-W11472 represent active Factor VIII:C analogues of the  
XX invention. These sequences were created by mutating the wild type Factor  
XX VIII:C coding sequence (see AAT5157) using mutagenic primers. The  
XX analogues comprise a native Factor VIII:C polypeptide modified at a site  
XX adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
XX dipeptide is created. Factor VIII:C is a large glycoprotein that  
XX participates in the blood coagulation cascade that ultimately converts  
XX soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
XX deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
XX X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
XX activated by plasma proteases, such as thrombin. During activation the  
XX mature polypeptide is cleaved to generate heavy and light chain fragments  
XX that are further cleaved. Complexes of two or more of the analogues,  
XX nucleic acids and vectors encoding them may be used alone or in  
XX conjunction with each other, for the prevention or treatment of active  
XX Factor VIII:C deficiency in a mammal. The analogues may be used as  
XX immunogens to raise antibodies, and in the treatment of haemophilias, by  
XX improvement of haemostasis. The analogues are resistant to proteolytic  
XX cleavage and display increased plasma half-life. They may be administered  
XX at lower dosages and by different modes of administration.  
XX  
XX Sequence 2349 AA:  
XX  
XX Query Match 99.8%; Score 12398; DB 18; Length 2349;  
XX Best Local Similarity 99.9%; Pred. No. 0;  
XX Matches 2349; Conservative 0; Mismatches 0; Indels 2; Gaps 1;  
XX  
XX 1 MOELSTCFCLRLRCFSATRRYVLGAVELSDMDYMSDGLGELPYDARPPRVKSPFN 60  
XX 1 MOELSTCFCLRLRCFSATRRYVLGAVELSDMDYMSDGLGELPYDARPPRVKSPFN 60  
XX 1 MOELSTCFCLRLRCFSATRRYVLGAVELSDMDYMSDGLGELPYDARPPRVKSPFN 60  
XX 61 TSVYKKTLEVEFTDHLFNIAKRPMMGLGPTIOAEYDVTITLNMASHVSLHAY 120  
XX  
XX 1139

61 TSVYKKTLEVEFTDHLFNIAKRPMMGLGPTIOAEYDVTITLNMASHVSLHAY 120  
121 GVSYWKASSEGAEYDDOTSOKEDEDDKVPGGSHHTYVQVLKENGPMASDPLCLTYSLSH 180  
121 GVSYWKASSEGAEYDDOTSOKEDEDDKVPGGSHHTYVQVLKENGPMASDPLCLTYSLSH 180  
181 VDLVYDNLNSGLIGALLVCREGSLAKERTQTLHFKTLFVAVDEGKSMSEETKNSLMODRD 240  
181 VDLVYDNLNSGLIGALLVCREGSLAKERTQTLHFKTLFVAVDEGKSMSEETKNSLMODRD 240  
241 AASARAPKMTYNGVYVNSLPLGLGCRKSVYVHTYMGCTTPVHSLFEGHFVLRNH 300  
241 AASARAPKMTYNGVYVNSLPLGLGCRKSVYVHTYMGCTTPVHSLFEGHFVLRNH 300  
301 ROASLEISPTFLTAOTLMDLMDGFLFCHTSHOHODGMEAYVYKSCPEBOLRMKNE 360  
301 ROASLEISPTFLTAOTLMDLMDGFLFCHTSHOHODGMEAYVYKSCPEBOLRMKNE 360  
361 EAEDYDDDLTDEMDVVRPDDNSPFIQIRSVAKKPKTKVHTYIAEEDMDYAPLYLA 420  
361 EAEDYDDDLTDEMDVVRPDDNSPFIQIRSVAKKPKTKVHTYIAEEDMDYAPLYLA 420  
421 PDDRSYKSOYLNNNGPORIGRKYKVRMAVYDTEFKTREAIQHESSGILGPLYGEVDTL 480  
421 PDDRSYKSOYLNNNGPORIGRKYKVRMAVYDTEFKTREAIQHESSGILGPLYGEVDTL 480  
481 LIFKNOASRPYNIYPHGTTDVRPLYSRRLPKGVKHLKDEPILPGEIFKYKMTVYEDGP 540  
481 LIFKNOASRPYNIYPHGTTDVRPLYSRRLPKGVKHLKDEPILPGEIFKYKMTVYEDGP 540  
479 LIIFKNOASRPYNIYHGTIDVRPLYSRRLPKGVKHLKDEPILPGEIFKYKMTVYEDGP 538  
541 TKSDPCLTRYSSFPNMRDLASGLIPPLICCKSVYQGRGNQJMSKRKRVILFSEVDE 600  
541 TKSDPCLTRYSSFPNMRDLASGLIPPLICCKSVYQGRGNQJMSKRKRVILFSEVDE 600  
539 TKSDPCLTRYSSFPNMRDLASGLIPPLICCKSVYQGRGNQJMSKRKRVILFSEVDE 598  
539 TKSDPCLTRYSSFPNMRDLASGLIPPLICCKSVYQGRGNQJMSKRKRVILFSEVDE 598  
601 NRSWLTENIORFLPNPAGVQLEDEFEQASNMHMSINGVYFDSLOLVCLHEVAVYVILS 660  
601 NRSWLTENIORFLPNPAGVQLEDEFEQASNMHMSINGVYFDSLOLVCLHEVAVYVILS 660  
661 IGAODHFLSVFSGYFVKRMYEDTLPLPFSGEYVPMSEMPGLMTLGGHNSDFPNRG 720  
661 IGAODHFLSVFSGYFVKRMYEDTLPLPFSGEYVPMSEMPGLMTLGGHNSDFPNRG 720  
659 IGAODHFLSVFSGYFVKRMYEDTLPLPFSGEYVPMSEMPGLMTLGGHNSDFPNRG 718  
659 IGAODHFLSVFSGYFVKRMYEDTLPLPFSGEYVPMSEMPGLMTLGGHNSDFPNRG 718  
721 MVALKYSQCDKMTGYEDSYEDISATVLSKNNALFPPSPQNSRHSSTOKOFNATY 780  
721 MVALKYSQCDKMTGYEDSYEDISATVLSKNNALFPPSPQNSRHSSTOKOFNATY 780  
719 MVALKYSQCDKMTGYEDSYEDISATVLSKNNALFPPSPQNSRHSSTOKOFNATY 778  
781 PENDIEKTDPMFAHRTPMKIONVSSSDILMLRKOSFTPHGLSLDLOEAKYETFSDDPS 840  
781 PENDIEKTDPMFAHRTPMKIONVSSSDILMLRKOSFTPHGLSLDLOEAKYETFSDDPS 840  
779 PENDIEKTDPMFAHRTPMKIONVSSSDILMLRKOSFTPHGLSLDLOEAKYETFSDDPS 838  
779 PENDIEKTDPMFAHRTPMKIONVSSSDILMLRKOSFTPHGLSLDLOEAKYETFSDDPS 838  
841 PGALDSNNLSSEMTHTRPQLHSGMPVTPESGLOLRNEMKIGTTAATELKKLDFKYSST 900  
841 PGALDSNNLSSEMTHTRPQLHSGMPVTPESGLOLRNEMKIGTTAATELKKLDFKYSST 900  
839 PGALDSNNLSSEMTHTRPQLHSGMPVTPESGLOLRNEMKIGTTAATELKKLDFKYSST 898  
839 PGALDSNNLSSEMTHTRPQLHSGMPVTPESGLOLRNEMKIGTTAATELKKLDFKYSST 898  
901 SNNLSTIPSDNLAAGTDNTSSLGPPSPVHYDSODTLTLFKKSSPLTEGSGPLSLEE 960  
901 SNNLSTIPSDNLAAGTDNTSSLGPPSPVHYDSODTLTLFKKSSPLTEGSGPLSLEE 960  
899 SNNLSTIPSDNLAAGTDNTSSLGPPSPVHYDSODTLTLFKKSSPLTEGSGPLSLEE 958  
899 SNNLSTIPSDNLAAGTDNTSSLGPPSPVHYDSODTLTLFKKSSPLTEGSGPLSLEE 958  
961 NNDGKLESGJMSQSSGKGVSTESGRLFGKRAHGPALTLFDNALFVYSILKTY 1020  
961 NNDGKLESGJMSQSSGKGVSTESGRLFGKRAHGPALTLFDNALFVYSILKTY 1020  
959 NNDGKLESGJMSQSSGKGVSTESGRLFGKRAHGPALTLFDNALFVYSILKTY 1018  
959 NNDGKLESGJMSQSSGKGVSTESGRLFGKRAHGPALTLFDNALFVYSILKTY 1018  
1021 KTSNNSATNRKTHIDPILLSLINSVWQNLISDTEFKKVPPLIHDMLMDKATATLRL 1080  
1021 KTSNNSATNRKTHIDPILLSLINSVWQNLISDTEFKKVPPLIHDMLMDKATATLRL 1080  
1019 KTSNNSATNRKTHIDPILLSLINSVWQNLISDTEFKKVPPLIHDMLMDKATATLRL 1078  
1019 KTSNNSATNRKTHIDPILLSLINSVWQNLISDTEFKKVPPLIHDMLMDKATATLRL 1078  
1081 NMSNKTTSKNNEMVQOKKEGPPIPPDQNDMSFPKMLFDESARMIORTHGKNSLNSG 1140  
1081 NMSNKTTSKNNEMVQOKKEGPPIPPDQNDMSFPKMLFDESARMIORTHGKNSLNSG 1140  
1079 NMSNKTTSKNNEMVQOKKEGPPIPPDQNDMSFPKMLFDESARMIORTHGKNSLNSG 1138  
1079 NMSNKTTSKNNEMVQOKKEGPPIPPDQNDMSFPKMLFDESARMIORTHGKNSLNSG 1138  
1141 OGSPKOLVSLGPEKVEGONFLSKKVVYVGGFTKDVGLKEVYFSSNLFITNLND 1200  
1141 OGSPKOLVSLGPEKVEGONFLSKKVVYVGGFTKDVGLKEVYFSSNLFITNLND 1200  
1139 OGSPKOLVSLGPEKVEGONFLSKKVVYVGGFTKDVGLKEVYFSSNLFITNLND 1198  
1139 OGSPKOLVSLGPEKVEGONFLSKKVVYVGGFTKDVGLKEVYFSSNLFITNLND 1198



QY	1201	LHENNTNHOEKKTOEIEETKEEPLLOEENVULPOIHVYTGKKNFNLEPLSTRONVBGSYD	1260
Db	1199	LHENNTNHOEKKTOEIEETKEEPLLOEENVULPOIHVYTGKKNFNLEPLSTRONVBGSYD	1258
QY	1261	GAYAVLADERSLNDSTNTRKKNTHAHSKSGEENLEJGNOQTOIYEKFACTRISPYT	1320
Db	1259	GAYAVLADERSLNDSTNTRKKNTHAHSKSGEENLEJGNOQTOIYEKFACTRISPYT	1318
QY	1321	SOONVYORSKRALKOFRLPLEETLEEKRIIYVDSTOWSKMKHLPRSLTOIDVNEKE	1380
Db	1319	SOONVYORSKRALKOFRLPLEETLEEKRIIYVDSTOWSKMKHLPRSLTOIDVNEKE	1378
QY	1381	KATIOSPISDCTREBHSIRPOANSPLPIAKVSSPSTIRPYTLRVLFONSSHLPASV	1440
Db	1379	KATIOSPISDCTREBHSIRPOANSPLPIAKVSSPSTIRPYTLRVLFONSSHLPASV	1438
QY	1441	RKKSQVOESSHPLQAKKNNLSALITLLEMTDQOREVSGTSTATNSVYTKKVENTYLP	1500
Db	1439	RKKSQVOESSHPLQAKKNNLSALITLLEMTDQOREVSGTSTATNSVYTKKVENTYLP	1498
QY	1501	KPDLPKTSQGVKELLPVNHYIYOKDLPETETSGSPGLDVBESGLQSTGEAIIKMNANP	1560
Db	1499	KPDLPKTSQGVKELLPVNHYIYOKDLPETETSGSPGLDVBESGLQSTGEAIIKMNANP	1558
QY	1561	GVPPRLVRAESSAKTPSKLLDPLAMNHNQTOIPEEEMKSOEKSPEKTAFFKKOTIISL	1620
Db	1559	GVPPRLVRAESSAKTPSKLLDPLAMNHNQTOIPEEEMKSOEKSPEKTAFFKKOTIISL	1618
QY	1621	NACESNHAIAINEGONKDEIVYMAKOGTERIKSONPPLYLKRHOEIRTRTLQDOEE	1680
Db	1619	NACESNHAIAINEGONKDEIVYMAKOGTERIKSONPPLYLKRHOEIRTRTLQDOEE	1678
QY	1681	IYDDTTSIVEMKEDDIDEDENOSPERSOKTRIFYFAAVERIMLYOGVSSPHYLYNR	1740
Db	1679	IYDDTTSIVEMKEDDIDEDENOSPERSOKTRIFYFAAVERIMLYOGVSSPHYLYNR	1738
QY	1741	AOSGSVPQPKVYVOEFTGSPFORVXGELNENHLLGLAPYRAVEDNIMVFFRQASR	1800
Db	1739	AOSGSVPQPKVYVOEFTGSPFORVXGELNENHLLGLAPYRAVEDNIMVFFRQASR	1798
QY	1801	PYSFYSLSLIEBEDQOGAEPPKKNFVKPNETIKTYFNKVONHMAPTKDEBCKAMAFESDY	1860
Db	1799	PYSFYSLSLIEBEDQOGAEPPKKNFVKPNETIKTYFNKVONHMAPTKDEBCKAMAFESDY	1858
QY	1861	DLEKDVHSGLLGRLVCHNTLNPAPHGROYVDEFLFTIPDEFKSNVFTENMENENCA	1920
Db	1859	DLEKDVHSGLLGRLVCHNTLNPAPHGROYVDEFLFTIPDEFKSNVFTENMENENCA	1918
QY	1921	PONIDMEPPRKEXYRERHAIINGYIMDTLPGLYMAOQORIRAWLILSMGSNENHISIFRSGH	1980
Db	1919	PONIDMEPPRKEXYRERHAIINGYIMDTLPGLYMAOQORIRAWLILSMGSNENHISIFRSGH	1978
QY	1981	VFTYVKKREKEMALYNLYRGVFEYEBMLPSKAGIMRYECLIGEBHLHAGMSTLFLVYSNK	2040
Db	1979	VFTYVKKREKEMALYNLYRGVFEYEBMLPSKAGIMRYECLIGEBHLHAGMSTLFLVYSNK	2038
QY	2041	QTPLOMASGIRFOITASGOYGOWAPKLARLHSGSINAMSTKPEFSWIKVLLAPMI	2100
Db	2039	QTPLOMASGIRFOITASGOYGOWAPKLARLHSGSINAMSTKPEFSWIKVLLAPMI	2098
QY	2101	HGKIKQAGROKFSKVIISOPIIMYSLDOCKMORYRGNISGTGLMVEFGVNDSSGKIKNIFN	2160
Db	2099	HGKIKQAGROKFSKVIISOPIIMYSLDOCKMORYRGNISGTGLMVEFGVNDSSGKIKNIFN	2158
QY	2161	PIPIARYIRLPHPHYSIRSTLPMELMGCDSLNSGMPLEKESKAISDQOITASSYPTNNPA	2220
Db	2159	PIPIARYIRLPHPHYSIRSTLPMELMGCDSLNSGMPLEKESKAISDQOITASSYPTNNPA	2218
QY	2221	TWSPKARLHLQGRSNANAPPOVNNKEMLQYDQCTMKTYTGVTYOGVKSLLTSMYKEPL	2280
Db	2219	TWSPKARLHLQGRSNANAPPOVNNKEMLQYDQCTMKTYTGVTYOGVKSLLTSMYKEPL	2278

Oy		2281-ISSSDGQHWTLFEFGKVKYPOGDSPFPVYNISLDEPLLTTRTALRHPSWVHDTALRM	2340
Dd		2279-ISSSDGGHWTLFEPNGKVVFQGNDSETPVVNSLDPELLRTILRIHQSWVHYDIALRM	2338
Oy		2341-EVLGCDAADLY	2351
Db		EVLGCDAADLY	2349
		RESULT_91 AAM10590 standard; protein; 2351 AA.	
XX		AAM10590;	
AC		03-DEC-1997 (first entry)	
DF		Factor VIII:C (Phe270His).	
XX		Factor VIIIC: F8C; Factor V A; Factor V C; domain; F8C deficiency; haemophilia A; blood clotting disorder; immunogen; antibody.	
KW		Homo sapiens.	
OS		Key Location/Qualifiers	
FH		Peptide 1..19	
FT		/note= "Signal peptide"	
FT		Protein 20..2351	
FT		/note= "Mature factor VIII:C"	
FT		Misc-difference 289 /label= Phe270His	
PX		WO9703191-A1.	
PD		30-JAN-1997.	
PF		28-JUN-1996; 96MO-US11013.	
PR		11-JUL-1995; 95US-0001030.	
PA		(CHIR ) CHIRON CORP.	
PI		Hung DT:	
DR		WFI: 1997-119047/11.	
PT		Factor VIII:C analogue - modified to comprise Factor V A or C domain or subdomain, for increased stability or activity	
PX		Claim 6; Page -: 45pp; English.	
CC		The sequences given in W10590-92 represent active Factor VIII:C (F8C) polypeptide analogues. These analogues comprises a native F8C polypeptide modified to comprise the presence of a Factor V A and/or C domain and/or subdomain. The F8C polypeptide analogues, alone or in combination, can be used for the prevention or treatment of an active F8C deficiency, i.e. haemophilia A and other blood clotting disorders. The analogue can also be used as an immunogen for antibody production. The analogues can have an increased plasma half-life, or specific activity. This sequence is not given in the specification and is based on the sequence derived from Genbank ref. K01740.	
SQ		Sequence 2351 AA:	
		Query Match 99.88; Score 12398; DB 18; Length 2351; Best Local Similarity 99.9%; Pred. No. 0; Matches 2348; Conservative 1; Mismatches 2; Indels 0; Gaps 0;	
Oy		I MOIELSTCFELLCRCFSATRRYYLGAVELSDMDYSGLGPVDARFFPPRVPKSFSPN	60
Db		I MOIELSTCFELLCRCFSATRRYYLGAVELSDMDYSGLGPVDARFFPPRVPKSFSPN	60
Oy		61 TSVYVKKTLFEETDLHPINAKRPDPMMGLGPTIOAEVYTGVITLNMAASHPVSLHAV	120

1141 OGPSPKOLVSLGPEKSEVGEONFLSEKKNVVGKGEFTKDVGLKEMVFPSSRNLFJLNDN 1200  
1201 LHENNTNHOEKKIOEIELEKTEKTLIOENVLNPQIHTVYTKNFKNLFLSTRONVEGSD 1260  
1201 LHENNTNHOEKKIOEIELEKTEKTLIOENVLNPQIHTVYTKNFKNLFLSTRONVEGSD 1260  
1261 GAYAPVLQDFRSLNDSTNRTKNTAHFSEKKEENLGLONQKQVEXYACTTISNT 1320  
1261 GAYAPVLQDFRSLNDSTNRTKNTAHFSEKKEENLGLONQKQVEXYACTTISNT 1320  
1321 SOONFVTOQRKRALQFRLPLEETELEKRIIVDDTSTOWSKNNKHLTPSTLQIDYNEKE 1380  
1321 SOONFVTOQRKRALQFRLPLEETELEKRIIVDDTSTOWSKNNKHLTPSTLQIDYNEKE 1380  
1381 KGATOSPFLDCLTRSHSPQANRSPPLAVSSPSTRPIYLRVLPQDNSSHPAPSY 1440  
1381 KGATOSPFLDCLTRSHSPQANRSPPLAVSSPSTRPIYLRVLPQDNSSHPAPSY 1440  
1441 RKDQSGVQESSHFLQAKKNLSLAILTEMTGDOREVSIGTSATNSVYKKEVNVLP 1500  
1441 RKDQSGVQESSHFLQAKKNLSLAILTEMTGDOREVSIGTSATNSVYKKEVNVLP 1500  
1501 KPDLPKTGKVELLPKHVYIOKDLPTERTSNGSGHLDYEGSLQGTGALIKMDEANRP 1560  
1501 KPDLPKTGKVELLPKHVYIOKDLPTERTSNGSGHLDYEGSLQGTGALIKMDEANRP 1560  
1561 GVPFLRVATESAKTPSKLLDPLANDNHYGTQIPKEBKSOEKSPEKTAFFKKTITSL 1620  
1561 GVPFLRVATESAKTPSKLLDPLANDNHYGTQIPKEBKSOEKSPEKTAFFKKTITSL 1620  
1621 NCESNHAIAINNGOKKPEIETVMAKQGRTERLCSQNPVLRKHOREITRTTLODQEE 1680  
1621 NCESNHAIAINNGOKKPEIETVMAKQGRTERLCSQNPVLRKHOREITRTTLODQEE 1680  
1681 IDYDITSEVKKEDPOTIYEDENOSPBFQKTKTHYTAIVETIMDYGSSPHYLRNR 1740  
1681 IDYDITSEVKKEDPOTIYEDENOSPBFQKTKTHYTAIVETIMDYGSSPHYLRNR 1740  
1741 AOGGSVPQFKVYQEFTEGDSFTQPYRGELEHNLGLGPYRAVEDNIMVTFRNQASR 1800  
1741 AOGGSVPQFKVYQEFTEGDSFTQPYRGELEHNLGLGPYRAVEDNIMVTFRNQASR 1800  
1801 PVSFTSLISTEEOGOCABPKNFKPMETTYKWKQVHMAATKQEPCKKMAVAFSPV 1860  
1801 PVSFTSLISTEEOGOCABPKNFKPMETTYKWKQVHMAATKQEPCKKMAVAFSPV 1860  
1861 DEKDVHSGLIGPLVYCHTNTLPNARGROYVQEBALFTTFDETKSWYTEMENRCHA 1920  
1861 DEKDVHSGLIGPLVYCHTNTLPNARGROYVQEBALFTTFDETKSWYTEMENRCHA 1920  
1921 PCNIOHEDETEKENRFAHNGYIMPTLGLVMAODORTIRYTLISMSNINISIHFSGH 1980  
1921 PCNIOHEDETEKENRFAHNGYIMPTLGLVMAODORTIRYTLISMSNINISIHFSGH 1980  
1981 VFTVRKKEEYKMAIYNLYPGVFETVEMLPSKAGINVRCLIGEHLHAGMSTFLVYASNC 2040  
1981 VFTVRKKEEYKMAIYNLYPGVFETVEMLPSKAGINVRCLIGEHLHAGMSTFLVYASNC 2040  
2041 QPPLGMAASHIRDPQITASGOYGOMAPKLABLHYSGSINAMSTKEPESWIKYDILAPMII 2100  
2041 QPPLGMAASHIRDPQITASGOYGOMAPKLABLHYSGSINAMSTKEPESWIKYDILAPMII 2100  
2101 HGIRTOGARQKSSLYISQFTIMSLDGKKWQYRKNSTGTLAMVFEFGVAVSGIKHINFN 2160  
2101 HGIRTOGARQKSSLYISQFTIMSLDGKKWQYRKNSTGTLAMVFEFGVAVSGIKHINFN 2160  
2161 PPIITARIYRLHPTHYSISITLRLMLCNDLNSCAMPGLGEMSKAISDAQITASSYFTNMPA 2220  
2161 PPIITARIYRLHPTHYSISITLRLMLCNDLNSCAMPGLGEMSKAISDAQITASSYFTNMPA 2220  
2221 TWSPSKARLHLQGRSANRPOVNNPKEMLOYDQKTKMYKTGYTTOGYVSLTSMYVVEFL 2280  
2221 TWSPSKARLHLQGRSANRPOVNNPKEMLOYDQKTKMYKTGYTTOGYVSLTSMYVVEFL 2280

Oy	2281	ISSSDQDHQWTLFFQNGKVKVPGQKQSPFVYNSSDPELTRYLRIHPQSWHQIALFM	2340
Db	2281	ISSSDQDHQWTLFFQNGKVKVPGQKQSPFVYNSSDPELTRYLRIHPQSWHQIALFM	2340
Oy	2341	EVLGCEADQDLY 2351	
Db	2341	EVLGCEADQDLY 2351	
RESULT 92			
ID	AAW11405	standard; Protein; 2350 AA.	
AC	AAW11405;		
XX	20-NOV-1997	(first entry)	
DE	Active Factor VIII:C analogue, delta 746, + 0744X.		
XX			
KW	Factor VIII:C; analogue; glycoprotein; blood coagulation cascade; fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis; plasma protease; thrombin; immunogen; antibody; haemophilicac; therapy; proteolytic cleavage.		
XX			
OS	Homo sapiens.		
XX	Synthetic.		
PH	Key	Location/Qualifiers	
FT	Peptide	1..19	
FT		/note="signal peptide"	
FT	Protein	20..2350	
FT		/note="mature Factor VIII:C"	
FT	Region	20..1666	
FT		/note="heavy chain fragment"	
FT	Modified-site	763	
FT		/label="Phe, Glu, Pro	
FT	Misc-difference	764..765	
FT		/note="site of 1 residue deletion"	
FT	Region	1667..2349	
FT		/note="light chain fragment"	
FT	Domain	759..1666	
FT		/note="B domain"	
XX			
PM	W09703195-A1.		
XX			
PD	30-JAN-1997.		
XX			
PF	09-JUL-1996;	96W0-US1444.	
XX			
PR	11-JUL-1995;	95US-0001025.	
XX			
PA	(CHIR ) CHIRON CORP.		
XX			
PI	Cohen FE, Hung DF, Innis M;		
DR	WPI. 1997-119050/11.		
XX			
PT	Factor VIII:C analog modified adjacent to a non-activating Arg		
PT	residue - used in the treatment of haemophilacs, by improvement of		
PT	haemostasis		
XX			
PS	Clalm 24, Page -: 90pp; English.		
XX			
CC	AAW11330-W11472 represent active Factor VIII:C analogues of the		
CC	invention. These sequences were created by mutating the wild type Factor		
CC	VIII:C coding sequence (see AAT51357) using mutagenic primers. The		
CC	analogues comprise a native Factor VIII:C polypeptide modified at a site		
CC	adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg		
CC	participle is created. Factor VIII:C is a large glycoprotein that		
CC	participates in the blood coagulation cascade that ultimately converts		
CC	soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A		
CC	deficiency in Factor VIII:C is responsible for haemophilia A, which is an		

Query Match	Best Local Similarity	Score	DB 18:	Length	2350:			
Matches 2349;	Conservative	0;	Mismatches	1;	Indels	1;	Gaps	1;
1	MOELSTFCFLICLRFCFSATRRYYLGAVELSMDYQMSDLAGELPYDAFRRPYKSPEN	60						
1	MOELSTFCFLICLRFCFSATRRYYLGAVELSMDYQMSDLAGELPYDAFRRPYKSPEN	60						
61	TSVYVKKTLPEPFIDHFNIAKPRPMWGLIGPTQAEYDVYVTLTKNMAHPVLSHV	120						
61	TSVYVKKTLPEPFIDHFNIAKPRPMWGLIGPTQAEYDVYVTLTKNMAHPVLSHV	120						
121	GVSYVKAESGAEDYDQTSOREKEDDKVFPGGSHYYVQYLKENGPMASDPLCLTYTSLH	180						
121	GVSYVKAESGAEDYDQTSOREKEDDKVFPGGSHYYVQYLKENGPMASDPLCLTYTSLH	180						
181	YQVYVMDLNSGLIGALLVYCRGSLAKKEKQTLHKPILFLVAFDEGKSMSEETKNSLMODBD	240						
181	YQVYVMDLNSGLIGALLVYCRGSLAKKEKQTLHKPILFLVAFDEGKSMSEETKNSLMODBD	240						
241	AAASAAMPKMTYGVYVNSLPGLLGCRKSVYVNYTGCTTPEVHSIFLEGHFLVLRNH	300						
241	AAASAAMPKMTYGVYVNSLPGLLGCRKSVYVNYTGCTTPEVHSIFLEGHFLVLRNH	300						
301	ROASLEISPIITLTAOTLLMDLQOPFLFCHTSSHQDHGMAYVYVDSCEPBPOLRMKNE	360						
301	ROASLEISPIITLTAOTLLMDLQOPFLFCHTSSHQDHGMAYVYVDSCEPBPOLRMKNE	360						
361	EAEEDYDQTLSEMDYVRFEDDONSPTQISVAKKPKPTWYVIAAEEEDMDAPLYLA	420						
361	EAEEDYDQTLSEMDYVRFEDDONSPTQISVAKKPKPTWYVIAAEEEDMDAPLYLA	420						
421	PDDRSYKQYVLANPQATIGKTKKYPMAVYDEFKTRKALQIHESGILGILLYGEVDTL	480						
421	PDDRSYKQYVLANPQATIGKTKKYPMAVYDEFKTRKALQIHESGILGILLYGEVDTL	480						
481	LIIFFKQASRPYNYIPGILTDVAPLYSRRLLPKGVKHLKDPILLPGEIFRYKWTYVEDG	540						
481	LIIFFKQASRPYNYIPGILTDVAPLYSRRLLPKGVKHLKDPILLPGEIFRYKWTYVEDG	540						
541	TSYSDPCLTRYYSFVMEBPDLASGLIGPLLYCKESVDQROGQIMSKRNVLLFSVDE	600						
541	TSYSDPCLTRYYSFVMEBPDLASGLIGPLLYCKESVDQROGQIMSKRNVLLFSVDE	600						
601	NRSWYLTENIORLPLNPAGVQLEDPEFOASINIMHSINGVYFDSLOSLVCLHEVAYTILS	660						
601	NRSWYLTENIORLPLNPAGVQLEDPEFOASINIMHSINGVYFDSLOSLVCLHEVAYTILS	660						
661	IGQVDFLSVFSGYGTAKHMYEDTLTFPFSGEYFVMSMEKPGMLILGCHNSDFENRG	720						
661	IGQVDFLSVFSGYGTAKHMYEDTLTFPFSGEYFVMSMEKPGMLILGCHNSDFENRG	720						
721	MPALLKVSCKNTGDYEDSYEDISAYILSKNNAIPRFSFNSNSHHSTOKOFNATTTI	780						
721	MPALLKVSCKNTGDYEDSYEDISAYILSKNNAIPRFSFNSNSHHSTOKOFNATTTI	780						
781	PENDIEKTDPMFAHRTMPKIONVSSDMLMLQOSTPTGILSLSDQBAKTEFFSDPS	840						
781	PENDIEKTDPMFAHRTMPKIONVSSDMLMLQOSTPTGILSLSDQBAKTEFFSDPS	840						
840	PENDIEKTDPMFAHRTMPKIONVSSDMLMLQOSTPTGILSLSDQBAKTEFFSDPS	840						

QY 841 PGALDSNNSLSBMTFHRPOLHSHSGDWFPPESGIOLRLNEKLGTTAATELKLDDFKVSSN 900  
DB 840 PGALDSNNSLSBMTFHRPOLHSHSGDWFTPESSQOLRLNEKLGTTAATELKLDDFKVSSN 899  
QY 901 SNNLISITIPSDMLAAGTDNTSSILGPPSMRVHYDSQDITTLTGKSSSPPTESGGPLSIEE 960  
DB 900 SNNLISITIPSDMLAAGTDNTSSILGPPSMRVHYDSQDITTLTGKSSSPPTESGGPLSIEE 959  
QY 961 NDSKILLESGLMNSQESSMGKNVSTESGRLFFGKRAHGPALLTMDNALFFVSIISLKTN 1020  
DB 960 NDSKILLESGLMNSQESSMGKNVSTESGRLFFGKRAHGPALLTMDNALFFVSIISLKTN 1019  
QY 1021 KTSNNSATNRKTHIDGSPLLIENSPSWONILSDTEFEKVTPLIHDMLMDKNAATLRL 1080  
DB 1020 KTSNNSATNRKTHIDGSPLLIENSPSWONILSDTEFEKVTPLIHDMLMDKNAATLRL 1079  
QY 1081 NMSNKTSSKNMENVQOKKEGPIPPDAONPDMSPFKMLFLPESARWIQTHGKNSLNSG 1140  
DB 1080 NMSNKTSSKNMENVQOKKEGPIPPDAONPDMSPFKMLFLPESARWIQTHGKNSLNSG 1139  
QY 1141 QGSPKQVSLGPEKSVBGONFLSEKKNVYVGGEFTKQVGLKEWFPSSRNLFITMDN 1200  
DB 1140 QGSPKQVSLGPEKSVBGONFLSEKKNVYVGGEFTKQVGLKEWFPSSRNLFITMDN 1199  
QY 1201 LHENNTHNOEKKIOEIEIEKKEKTLIOENVVLPQIHTVYGTGRNFMKMLFLSTRONVEGSD 1260  
DB 1200 LHENNTHNOEKKIOEIEIEKKEKTLIOENVVLPQIHTVYGTGRNFMKMLFLSTRONVEGSD 1259  
QY 1261 GATAPVLOPFRSLNSTNRKTHAHFSKKGEEENLEJGNGOTKOIVKRYACTRISPT 1320  
DB 1260 GATAPVLOPFRSLNSTNRKTHAHFSKKGEEENLEJGNGOTKOIVKRYACTRISPT 1319  
QY 1321 SQONFVYQSRKRALQKQFLPLEETELEKRIIVDTSTOWSKNNKHLPSLTLQIDYNEKE 1380  
DB 1320 SQONFVYQSRKRALQKQFLPLEETELEKRIIVDTSTOWSKNNKHLPSLTLQIDYNEKE 1379  
QY 1381 KGATOSPDLDCITRHSHPQANRSPPLIAKVSFSPSIRIYITRYLFCODNSHLPAASY 1440  
DB 1380 KGATOSPDLDCITRHSHPQANRSPPLIAKVSFSPSIRIYITRYLFCODNSHLPAASY 1439  
QY 1441 RKKDSVOESSHFLQAKAKNNLSLAILTLEMTGDQREVSGLSATNSVYTKKVENYVLP 1500  
DB 1440 RKKDSVOESSHFLQAKAKNNLSLAILTLEMTGDQREVSGLSATNSVYTKKVENYVLP 1499  
QY 1501 KPDLPTSGVVELLPVHYIYOKDLPPTETSGSPGHLDVEGSLQGTGCAIKMEANRP 1560  
DB 1500 KPDLPTSGVVELLPVHYIYOKDLPPTETSGSPGHLDVEGSLQGTGCAIKMEANRP 1559  
QY 1561 GKVPFLRVATESAKTPSKLDDPLAMDNHYGTQIPKEEMKSQEKSPKTAFFKKDITLST 1620  
DB 1560 GKVPFLRVATESAKTPSKLDDPLAMDNHYGTQIPKEEMKSQEKSPKTAFFKKDITLST 1619  
QY 1621 NACSNHAIAINEGONKPEIEVTAQKGRTERLCSONPVYLKRHRQRETTITLQSDQEE 1680  
DB 1620 NACSNHAIAINEGONKPEIEVTAQKGRTERLCSONPVYLKRHRQRETTITLQSDQEE 1679  
QY 1681 IDYDDTISVEMKEDDPIYDEDENOSPSPSFOKTRHFFIAAVERLMDYKASSPVLNLR 1740  
DB 1680 IDYDDTISVEMKEDDPIYDEDENOSPSPSFOKTRHFFIAAVERLMDYKASSPVLNLR 1739  
QY 1741 AQSGSVPQFKKVVFOEFTGDSFTQPLRYGELNEHLGLGPIYIAEVEDINWTFPNQASR 1800  
DB 1740 AQSGSVPQFKKVVFOEFTGDSFTQPLRYGELNEHLGLGPIYIAEVEDINWTFPNQASR 1799  
QY 1801 PYSFYSSLIISTEBDQOGAEPKRNKYNKNETKITFKKVOHNAAPYDEDFDCAKAAVFEVD 1860  
DB 1800 PYSFYSSLIISTEBDQOGAEPKRNKYNKNETKITFKKVOHNAAPYDEDFDCAKAAVFEVD 1859  
QY 1861 DLEKDVHSGGLGLPLVCHNTNLNPAHGRQVYVOEFALFTIIPDETSMWTFENMERNCRA 1920  
DB 1860 DLEKDVHSGGLGLPLVCHNTNLNPAHGRQVYVOEFALFTIIPDETSMWTFENMERNCRA 1919

QY 1921 PONTIOMEDPTEKENTRERHAINCYIMDTPLGLVMAODORIRWYLLSMGSENHISIHFSGH 1980  
DB 1920 PONTIOMEDPTEKENTRERHAINCYIMDTPLGLVMAODORIRWYLLSMGSENHISIHFSGH 1979  
QY 1981 VFTYAKKEEYKMLNLYNGVFEYEBMLPSKAGIMRECECLIGEHLHAGSTLFLVYSNKC 2040  
DB 1980 VFTYAKKEEYKMLNLYNGVFEYEBMLPSKAGIMRECECLIGEHLHAGSTLFLVYSNKC 2039  
QY 2041 QTPLGMAHGRIDFQITASGOYGOAAPKLARLHYSGSINASTKEPFWIKVDLAPMI 2100  
DB 2040 QTPLGMAHGRIDFQITASGOYGOAAPKLARLHYSGSINASTKEPFWIKVDLAPMI 2099  
QY 2101 HGKIKQAGROKFSLSYISOPFIIMYSLDGKKQYTRGNSGTGLWVFFGNDSSGKIHNIEN 2160  
DB 2100 HGKIKQAGROKFSLSYISOPFIIMYSLDGKKQYTRGNSGTGLWVFFGNDSSGKIHNIEN 2159  
QY 2161 PPIIARYIRLHPHYSTRSLRMEIMGCDLNSCAMPJGMSKASIDAOITASSYTNMFA 2220  
DB 2160 PPIIARYIRLHPHYSTRSLRMEIMGCDLNSCAMPJGMSKASIDAOITASSYTNMFA 2219  
QY 2221 TWSPSKARLHLOGRSNAMPQVNNPKEMLOVDFOKTMKVYGVTTQGVKSILTSMTYKEFL 2280  
DB 2220 TWSPSKARLHLOGRSNAMPQVNNPKEMLOVDFOKTMKVYGVTTQGVKSILTSMTYKEFL 2279  
QY 2281 ISSSODGHQMTLFFQONKQVYFQGNDSFTPVNSLDPPLITRYLRHPOSWHODIALRM 2340  
DB 2280 ISSSODGHQMTLFFQONKQVYFQGNDSFTPVNSLDPPLITRYLRHPOSWHODIALRM 2339  
QY 2341 EVLGCEAODLY 2351  
DB 2340 EVLGCEAODLY 2350

RESULT 93  
AAM11346  
ID AAM11346 standard; Protein: 2350 AA.  
XX  
XX AAM11346;  
DE 17-NOV-1997 (first entry)  
XX  
XX  
XX Active Factor VIII:C analogue, delta 251, 252, + Pro Insertion.  
DE  
XX Factor VIII:C; analogue: glycoprotein; blood coagulation cascade;  
XX fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KW plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;  
KW proteolytic cleavage.  
XX  
XX Homo sapiens.  
OS  
XX Synthetic.  
XX  
XX  
XX Key Location/Qualifiers  
FH Peptide 1..19  
FT /note= "signal peptide"  
FT Protein 20..2350  
FT /note= "mature Factor VIII:C"  
FT Region 20..1666  
FT /note= "heavy chain fragment"  
FT Misc-difference 269..270  
FT /note= "site of 2 residue deletion"  
FT /note= "inserted residue"  
FT Region 1667..2349  
FT /note= "light chain fragment"  
FT Domain 759..1666  
FT /note= "B domain"  
XX  
XX W09703195-A1.  
XX  
XX 30-JAN-1997.  
XX  
XX 09-JUL-1996; 96W0-US11444.  
XX



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Db      1560 GAYPFLKATTESSAKTPSKLLDPLADNHNHGVQIRKEMKQSEKSPKTAFFKKKDLITSL 1619
Oy      1621 NACESNHAIAININSONKPEIEVTWAKOGTERLCSQNPVYLKRRQREITRTLLQSDQEE 1680
Db      1620 NACESNHAIAIAININSONKPEIEVTWAKOGTERLCSQNPVYLKRRQREITRTLLQSDQEE 1679
Oy      1681 IDYDPTISVEMKKEDFDIYDEDENSPSPFOKTRHYFAAVERLMDYGMSSPHVLRNR 1740
Db      1680 IDYDPTISVEMKKEDFDIYDEDENSPSPFOKTRHYFAAVERLMDYGMSSPHVLRNR 1739
Oy      1741 AQSASVPQKRVVPPEFDGTFQPLRGELNHHGLGCPYRAEVENIMVFERNDASR 1800
Db      1740 AQSASVPQKRVVPPEFDGTFQPLRGELNHHGLGCPYRAEVENIMVFERNDASR 1799
Oy      1801 PYSFYSLLSYEDDQROGAEPBRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAMAYFSDY 1860
Db      1800 PYSFYSLLSYEDDQROGAEPBRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAMAYFSDY 1859
Oy      1861 DLEKDVHSLIGLPLVCHTNTLNPAHGRQYVQEFALFTIDETKSWYFTENNERCRA 1920
Db      1860 DLEKDVHSLIGLPLVCHTNTLNPAHGRQYVQEFALFTIDETKSWYFTENNERCRA 1919
Oy      1921 PCNIOMEDPTFEKNYRFAHNGYIMDTLPGIYVADQORIRWYLLSGNSNENIHSIHFSGH 1979
Db      1920 PCNIOMEDPTFEKNYRFAHNGYIMDTLPGIYVADQORIRWYLLSGNSNENIHSIHFSGH 1979
Oy      1981 VFTYVRKKEEYKMAKLVNIPGVETVEMLPKAGIMVRECLIGENLHAGMSTLFLVYSNKC 2040
Db      1980 VFTYVRKKEEYKMAKLVNIPGVETVEMLPKAGIMVRECLIGENLHAGMSTLFLVYSNKC 2039
Oy      2041 QTPIGMASGHIRDFQITASGOYGMAPKRLARLHSSGINASTKEPFSKIVDLAEMIT 2100
Db      2040 QTPIGMASGHIRDFQITASGOYGMAPKRLARLHSSGINASTKEPFSKIVDLAEMIT 2099
Oy      2101 HGITQGARQKFSSLYISQFIIMYSIDQKKMOTYRGNSGTGLVFEFGVNDSSGIKHNIFN 2160
Db      2100 HGITQGARQKFSSLYISQFIIMYSIDQKKMOTYRGNSGTGLVFEFGVNDSSGIKHNIFN 2159
Oy      2161 PPIIARIIRLPHPHYSIRSTLMEMLGCDLNSCMPMGESKRAISPAQITASSFTNMA 2220
Db      2160 PPIIARIIRLPHPHYSIRSTLMEMLGCDLNSCMPMGESKRAISPAQITASSFTNMA 2219
Oy      2221 TWSPSKARLHLOGRSNAMPQVNNPKEWLQVDFQTKMKTGYVTTOGVSLLTSMYKEFL 2280
Db      2220 TWSPSKARLHLOGRSNAMPQVNNPKEWLQVDFQTKMKTGYVTTOGVSLLTSMYKEFL 2279
Oy      2281 ISSSODGHQWTLFFQNGKXKVFQGNQDSFTPYVNSLDPPLITRYLRIHQPSVWHQIALRM 2340
Db      2280 ISSSODGHQWTLFFQNGKXKVFQGNQDSFTPYVNSLDPPLITRYLRIHQPSVWHQIALRM 2339
Oy      2341 EVLGECAQDLY 2351
Db      2340 EVLGECAQDLY 2350

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RESULT 94  
AAW11470  
ID AAW11470 standard; Protein; 2350 AA.

AAW11470;  
21-NOV-1997 (first entry)  
Active Factor VIII:C analogue, delta 1720, + L1718X.  
Factor VIII:C analogue; glycoprotein; blood coagulation cascade;  
fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
plasma protease; thrombin; immunogen; antibody; haemophilia; therapy;  
proteolytic cleavage.  
Homo sapiens.  
Synthetic.

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XX      Key Location/Qualifiers
FH      Peptide 1..19
FT      Protein /note="signal peptide"
FT      Region 20..2350
FT      Region /note="mature Factor VIII:C"
FT      Region 20..1667
FT      Region /note="heavy chain fragment"
FT      Domain 1668..2349
FT      Domain /note="light chain fragment"
FT      Domain 759..1667
FT      Domain /note="B domain"
FT      Modified-site 1737
FT      /label= Phe, Glu, Pro
FT      Misc-difference 1738..1739
FT      /note="site of 1 residue deletion"
XX      WO9703195-A1.
XX      30-JAN-1997.
XX      09-JUL-1996; 96WO-US11444.
XX      11-JUL-1995; 95US-0001025.
XX      (CHIR ) CHIRON CORP.
XX      Cohen FE, Hung DT, Innis M;
XX      WPI; 1997-119050/11.
XX      Factor VIII:C analog modified adjacent to a non-activating Arg
XX      residue - used in the treatment of haemophilias, by improvement of
XX      haemostasis
XX      Claim 38; Page -: 90pp; English.
XX      AAW11330-W11472 represent active Factor VIII:C analogues of the
XX      invention. These sequences were created by mutating the wild type Factor
XX      VIII:C coding sequence (see AAT51357) using mutagenic primers. The
XX      analogues comprise a native Factor VIII:C polypeptide modified at a site
XX      adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
XX      dipeptide is created. Factor VIII:C is a large glycoprotein that
XX      participates in the blood coagulation cascade that ultimately converts
XX      soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
XX      deficiency in Factor VIII:C is responsible for haemophilia A, which is an
XX      X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
XX      activated by plasma proteases, such as thrombin. During activation the
XX      mature polypeptide is cleaved to generate heavy and light chain fragments
XX      that are further cleaved. Complexes of two or more of the analogues,
XX      nucleic acids and vectors encoding them may be used alone or in
XX      conjunction with each other, for the prevention or treatment of active
XX      Factor VIII:C deficiency in a mammal. The analogues may be used as
XX      immunogens to raise antibodies, and in the treatment of haemophilias, by
XX      improvement of haemostasis. The analogues are resistant to proteolytic
XX      cleavage and display increased plasma half-life. They may be administered
XX      at lower dosages and by different modes of administration.
XX      Sequence 2350 AA:
SQ      Query Match 99.8%; Score 12396.5; DB 18; Length 2350;
XX      Best Local Similarity 99.9%; Pred. No. 0;
XX      Matches 2349; Conservative 0; Mismatches 1; Indels 1; Gaps 1;
Oy      1 MOJETSTCFCLLRFCSATRRYVLAGAVELSWDYQSDGLGELPYDARFPPRPVKSFPFN 60
Db      1 MOJETSTCFCLLRFCSATRRYVLAGAVELSWDYQSDGLGELPYDARFPPRPVKSFPFN 60
Oy      61 TSVYVYKRTLFVFEFTHLNINAKPRPPMGILGPTIOAEYDVTYVTLTKNNA5HPVSLHAY 120
Db      61 TSVYVYKRTLFVFEFTHLNINAKPRPPMGILGPTIOAEYDVTYVTLTKNNA5HPVSLHAY 120
Oy      121 GVSVMKASGAEYDDQTSREKEDKVPFGSHYVYQVLKENGPMASDPLCTYSLSH 180

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121 GSVYKASEGAEYDDQSOKEKEDKVPFGSGSHYYWQVLKENGPMASDPCLCTFYSLSH 180  
181 VDLVKDNLNSGLIGALLVCREGSLAKEKTQTHKTLIFAPFBGSGSWSEPKNSLMDRD 240  
181 VDLVKDNLNSGLIGALLVCREGSLAKEKTQTHKTLIFAPFBGSGSWSEPKNSLMDRD 240  
241 AASARAMPKMHVYNGVYVNSRLPGLLGCHRSVYVHWIYGMGTTPVHSTIFLEGHTFLVNH 300  
241 AASARAMPKMHVYNGVYVNSRLPGLLGCHRSVYVHWIYGMGTTPVHSTIFLEGHTFLVNH 300  
301 ROASLEISDEPFLTAOTLMDGQFLFCHSHSHQHDGMEAVYKVDSCPEEPOLRMKNNE 360  
301 ROASLEISDEPFLTAOTLMDGQFLFCHSHSHQHDGMEAVYKVDSCPEEPOLRMKNNE 360  
361 EAEYDDDLTDSMDVYRRPDDNSPSFIOIRSVAKKHKPTWYHYAAEEDMDYAPLYLA 420  
361 EAEYDDDLTDSMDVYRRPDDNSPSFIOIRSVAKKHKPTWYHYAAEEDMDYAPLYLA 420  
421 PDDRSYKSQYLLNNGPQIRGKYYKVRMAVYDETFKTRREALIOHESGILGPELLYGEVDTL 480  
421 PDDRSYKSQYLLNNGPQIRGKYYKVRMAVYDETFKTRREALIOHESGILGPELLYGEVDTL 480  
481 LIIFFKNOASRPYNIYPHIGITDVRPLYSRRLPKGVKHLKOPPLIPGIFKYYKWTYVEDGP 540  
481 LIIFFKNOASRPYNIYPHIGITDVRPLYSRRLPKGVKHLKOPPLIPGIFKYYKWTYVEDGP 540  
541 TKSDPRCLTRYSSFPVMMERDLASGLIGPLLICRYKESVDORGQIMSDKRNVIIFYVDE 600  
541 TKSDPRCLTRYSSFPVMMERDLASGLIGPLLICRYKESVDORGQIMSDKRNVIIFYVDE 600  
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601 NRSWYLTENIORFLPNPAGVLEDEPEFOASNIMHSINGVYFDSLQSLVCLHEVAYWYLS 660  
661 IGAOTDFLSVFESEGYFHKHMYEDTLTPPSEGEYFVMSMEBGMITIGCHNSPFRRG 720  
661 IGAOTDFLSVFESEGYFHKHMYEDTLTPPSEGEYFVMSMEBGMITIGCHNSPFRRG 720  
721 MTALLKYSCKDKNTGQYTEDSTEDISAYLKSNNALIEPRSFSONSRHSPSTROKOPNATTI 780  
721 MTALLKYSCKDKNTGQYTEDSTEDISAYLKSNNALIEPRSFSONSRHSPSTROKOPNATTI 780  
781 PENDIEKTDPMFAHRTPMKPIQVNSSSDLMLNQSPTPHGLSLSDLOAKYETFSDDPS 840  
781 PENDIEKTDPMFAHRTPMKPIQVNSSSDLMLNQSPTPHGLSLSDLOAKYETFSDDPS 840  
841 PGATDSNNSISEMTHPRPOLHSGDMVFTPESSGLOLRNKLGTATATLTKLDDPKVYST 900  
841 PGATDSNNSISEMTHPRPOLHSGDMVFTPESSGLOLRNKLGTATATLTKLDDPKVYST 900  
901 SNMLISTIPSDNLAAGTNTSSLGPPSPMVHYDSQLDTLFGKSSPLTESGGLSISEE 960  
901 SNMLISTIPSDNLAAGTNTSSLGPPSPMVHYDSQLDTLFGKSSPLTESGGLSISEE 960  
961 NNDKLESGGLMNSOESSMGKNVSTESGRLFKGRRAHGPALLTKONALFKVYSILKTN 1020  
961 NNDKLESGGLMNSOESSMGKNVSTESGRLFKGRRAHGPALLTKONALFKVYSILKTN 1020  
1021 KTSNNSAATNRKTHIDGSLIENSFWQNLIESPTFKVYPLIDHRLMLKNAATLRL 1080  
1021 KTSNNSAATNRKTHIDGSLIENSFWQNLIESPTFKVYPLIDHRLMLKNAATLRL 1080  
1081 NMSNRKTTSSKNMDEWQKKEGPIPPDAQNDPMSEFKMLFLPSASAWIORTGKNSLSNG 1140  
1081 NMSNRKTTSSKNMDEWQKKEGPIPPDAQNDPMSEFKMLFLPSASAWIORTGKNSLSNG 1140  
1141 OGSPSPKOLVSLGPEKSVEGONFLSEKNKVVYVGKEFTKDVGLBMYPPSRNLFLTNJDN 1200  
1141 OGSPSPKOLVSLGPEKSVEGONFLSEKNKVVYVGKEFTKDVGLBMYPPSRNLFLTNJDN 1200  
1201 LHENNTHNOEKKIOEBIEKEKTLIOENVVLPQIHTVYGTKNFKMLFLSTRQNVESGYD 1260  
1201 LHENNTHNOEKKIOEBIEKEKTLIOENVVLPQIHTVYGTKNFKMLFLSTRQNVESGYD 1260

1201 LHENNTHNOEKKIOEBIEKEKTLIOENVVLPQIHTVYGTKNFKMLFLSTRQNVESGYD 1260  
1261 GAYAVLQDFRSLNDSTNRTKKHTAHFSKSGEENLEGLOTKOIVEXACTPRISPNT 1320  
1261 GAYAVLQDFRSLNDSTNRTKKHTAHFSKSGEENLEGLOTKOIVEXACTPRISPNT 1320  
1321 SOONTVOTRSKRALKQRLPLEETLEKRIIYVDTSTOWSKNKHLPSTGLQIDYNEKE 1380  
1321 SOONTVOTRSKRALKQRLPLEETLEKRIIYVDTSTOWSKNKHLPSTGLQIDYNEKE 1380  
1381 KGAITOSPCLSTRSHSIPOANRSPPLIAKVSSFPISIRYILTRVLPQDONSMLPAASY 1440  
1381 KGAITOSPCLSTRSHSIPOANRSPPLIAKVSSFPISIRYILTRVLPQDONSMLPAASY 1440  
1441 RKKGSGVOESSHFLQAGKKNKNSLAILTEMTQGOAREVSLGTSATNSVYKKEVNTLP 1500  
1441 RKKGSGVOESSHFLQAGKKNKNSLAILTEMTQGOAREVSLGTSATNSVYKKEVNTLP 1500  
1501 KPDLPKTSGKVELLPKVHIYQNDLPETTSNGSPGHLDLYEGSLQGTGCAIKMNEANRP 1560  
1501 KPDLPKTSGKVELLPKVHIYQNDLPETTSNGSPGHLDLYEGSLQGTGCAIKMNEANRP 1560  
1561 GAVPFLRVATESSAKTPSKLLDPLAUNDHNGTQIPKEBMSQEKSPKTAFAKKDITLSL 1620  
1561 GAVPFLRVATESSAKTPSKLLDPLAUNDHNGTQIPKEBMSQEKSPKTAFAKKDITLSL 1620  
1621 NACESNHAIAAINEGOKKPELTYTNAKQGRTERLCSOPRVLKHOERLITRTTLOSDEE 1680  
1621 NACESNHAIAAINEGOKKPELTYTNAKQGRTERLCSOPRVLKHOERLITRTTLOSDEE 1680  
1681 IDYDDTISEMKEEDFDIYDEDENOSPRSFOKTRHYFIAVERLWDYGMSSSPHVLNR 1740  
1681 IDYDDTISEMKEEDFDIYDEDENOSPRSFOKTRHYFIAVERLWDYGMSSSPHVLNR 1740  
1741 AOSGSVPQFKVQFQETDGSFPQYLRRELLENHGLGPIYRAEVEDNIWYTFPNOASR 1800  
1741 AOSGSVPQFKVQFQETDGSFPQYLRRELLENHGLGPIYRAEVEDNIWYTFPNOASR 1800  
1740 AOSGSVPQFKVQFQETDGSFPQYLRRELLENHGLGPIYRAEVEDNIWYTFPNOASR 1799  
1801 PYSFYSLSLISTEEOQROGAPRNKPNFKPMTKTYFKVYQVHMAPTDDEPDCAAKAFESDV 1860  
1801 PYSFYSLSLISTEEOQROGAPRNKPNFKPMTKTYFKVYQVHMAPTDDEPDCAAKAFESDV 1860  
1861 DLEKDVHSGLLGPLLVCHTNTLNPAGROVYVQEFALFTTIFDETYSWYFTENMBRNCRA 1920  
1861 DLEKDVHSGLLGPLLVCHTNTLNPAGROVYVQEFALFTTIFDETYSWYFTENMBRNCRA 1920  
1920 PCNIDMEDPTKENYRPHAINGYIMDTLPGVMAODORIRMYLLSMGSENDHSHIFSGH 1980  
1920 PCNIDMEDPTKENYRPHAINGYIMDTLPGVMAODORIRMYLLSMGSENDHSHIFSGH 1980  
1981 VFTYVRKKEBYKMALYNLYPCGVFETVEMLPKSKAGIWRBECLEGHLAAGSTLFLVYSMKC 2040  
1981 VFTYVRKKEBYKMALYNLYPCGVFETVEMLPKSKAGIWRBECLEGHLAAGSTLFLVYSMKC 2040  
2040 QYPLGASGHLRDPQITASQOYQAMPKLARLHSGSINASTKEPMSIKYDLLAPMI 2099  
2040 QYPLGASGHLRDPQITASQOYQAMPKLARLHSGSINASTKEPMSIKYDLLAPMI 2099  
2101 HGKTOGAKROKFPSSLYISQFTIYSLDGKMKQTYGNSGTGLAMFPGVNDSSGIGHNIFN 2160  
2101 HGKTOGAKROKFPSSLYISQFTIYSLDGKMKQTYGNSGTGLAMFPGVNDSSGIGHNIFN 2160  
2161 PPIIAYIRLHPHYSTIRSTLRMELWGCJLNSCSNPLMGESKASIDQAITYASSYFTNNFA 2220  
2161 PPIIAYIRLHPHYSTIRSTLRMELWGCJLNSCSNPLMGESKASIDQAITYASSYFTNNFA 2220  
2221 TWSPSKARLHLOGRSNMRPOVNNPKEMLOVDFOKTMYVTYTOGKSLTSMVYKFEFL 2280  
2221 TWSPSKARLHLOGRSNMRPOVNNPKEMLOVDFOKTMYVTYTOGKSLTSMVYKFEFL 2280  
2281 ISSSDQGHQWTLFPQONKXVYFQGNDSSTPYVNSLDPLLTRILRLHPOQSVHQAIALRM 2340  
2281 ISSSDQGHQWTLFPQONKXVYFQGNDSSTPYVNSLDPLLTRILRLHPOQSVHQAIALRM 2340  
2380 ISSSDQGHQWTLFPQONKXVYFQGNDSSTPYVNSLDPLLTRILRLHPOQSVHQAIALRM 2399

Oy 2341 EVLGEADPLY 2351  
|||||  
Db 2340 EVLGEADPLY 2350

RESULT 95  
AAW1375  
ID AAW1375 standard; Protein: 2350 AA.  
XX AAW1375;  
AC  
XX  
Df 18-NOV-1997 (first entry)  
XX  
XX Active Factor VIII:C analogue, delta 337, 338, + Pro insertion.  
XX  
XX Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;  
XX fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
XX plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;  
XX proteolytic cleavage.  
XX  
XX Homo sapiens.  
OS Synthetic.  
XX  
XX Key Location/Qualifiers  
FH Peptide 1..19  
FT /note= "signal peptide"  
FT 20..2350  
FT Protein /note= "mature Factor VIII:C"  
FT 20..1666  
FT Region /note= "heavy chain fragment"  
FT Misc-difference 355..356  
FT /note= "site of 2 residue deletion"  
FT Misc-difference 356  
FT /note= "inserted residue"  
FT Region 1667..2349  
FT /note= "light chain fragment"  
FT 759..1666  
FT Domain /note= "B domain"  
XX  
XX W09703195-A1.  
XX  
XX 30-JAN-1997.  
XX  
XX 09-JUL-1996; 96MO-US11444.  
XX  
XX 11-JUL-1995; 950S-0001025.  
XX  
XX (CHIR ) CHIRON CORP.  
XX  
XX Cohen FE, Hung DT, Innis M;  
PI WPI, 1997-119050/11.  
XX  
XX Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophiliacs, by improvement of  
PT haemostasis  
XX  
XX  
XX Claim 17; Page -: 90pp; English.  
XX  
XX AAW1330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,

CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophiliacs, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX  
XX  
XX Sequence 2350 AA:  
SQ

Query Match 99.8%; Score 12396.5; DB 18; Length 2350;  
Best Local Similarity 99.9%; Pred. NO. 0;  
Matches 2349; Conservative 0; Mismatches 1; Indels 1; Gaps 1;

Oy 1 MOELSTCFPLCLIRCFSTARRYLGAVELSMQSDGLPVDAREPPVAPKSPFFN 60  
Db 1 MOELSTCFPLCLIRCFSTARRYLGAVELSMQSDGLPVDAREPPVAPKSPFFN 60  
Oy 61 TSYYKKTLFEFTDHLFNIAKPRPPMGLGPTTQAEVYDVTYITLKMASHPVSLHAY 120  
Db 61 TSYYKKTLFEFTDHLFNIAKPRPPMGLGPTTQAEVYDVTYITLKMASHPVSLHAY 120  
Oy 121 GSYWKASGEAEYDDOTSOREKEDKVPFGSHTYVQVLKENGPMASDPLCLTVSYLSH 180  
Db 121 GSYWKASGEAEYDDOTSOREKEDKVPFGSHTYVQVLKENGPMASDPLCLTVSYLSH 180  
Oy 181 VDLVKDLSGLIGALLVCBRSGLAKETOTLHKTLLFANFDEGKSHSETKNSLMODRD 240  
Db 181 VDLVKDLSGLIGALLVCBRSGLAKETOTLHKTLLFANFDEGKSHSETKNSLMODRD 240  
Oy 241 AASARAPKMTYVGVYNSRLPGLGCHRSKYVYHVGMTPEVHSIFLECHTELVANH 300  
Db 241 AASARAPKMTYVGVYNSRLPGLGCHRSKYVYHVGMTPEVHSIFLECHTELVANH 300  
Oy 301 ROSLEISPIFTLAOTLLMDLQGLTCHSSHQHGMAYKVNSCEPEPOLMKKNE 360  
Db 301 ROSLEISPIFTLAOTLLMDLQGLTCHSSHQHGMAYKVNSCEPEPOLMKKNE 360  
Oy 361 EADYDDDLTDEMDVYRFDNDSFQIIRSVAKHPKTVHVIAAEEDMDYAPLYA 420  
Db 361 EADYDDDLTDEMDVYRFDNDSFQIIRSVAKHPKTVHVIAAEEDMDYAPLYA 420  
Oy 421 PDRSYKQYLNNGPQIGKRYKVFAYATDEPKPEALOHESGILPILXGEYDPL 480  
Db 421 PDRSYKQYLNNGPQIGKRYKVFAYATDEPKPEALOHESGILPILXGEYDPL 480  
Oy 481 LIIFKNOASRPYNIYPGIDVAPLYSRRLPKGVKHLKDPILLEGELFKYKMTVYEDGP 540  
Db 481 LIIFKNOASRPYNIYPGIDVAPLYSRRLPKGVKHLKDPILLEGELFKYKMTVYEDGP 540  
Oy 541 TSDPRLCLTRYSSFFVMMERDLASGLIGPLLCYKESVDQGNQIMSDKNVILFSPDE 600  
Db 541 TSDPRLCLTRYSSFFVMMERDLASGLIGPLLCYKESVDQGNQIMSDKNVILFSPDE 600  
Oy 601 NRSWYLTENIQRLPNPAGVQLEDPFOASNTMHSINGVYFDSIQLSVCLHAYAYT 660  
Db 601 NRSWYLTENIQRLPNPAGVQLEDPFOASNTMHSINGVYFDSIQLSVCLHAYAYT 660  
Oy 661 IGAQIDELSVFSGYTRKHMYVEDTLTFPSGTEVPMENMGMLILGCHNSDRNRG 720  
Db 661 IGAQIDELSVFSGYTRKHMYVEDTLTFPSGTEVPMENMGMLILGCHNSDRNRG 720  
Oy 720 MVALKVSCKDNKGDEYEDISAYILSKNNNAIEPRSSQNSRPSRQOFNATTI 780  
Db 720 MVALKVSCKDNKGDEYEDISAYILSKNNNAIEPRSSQNSRPSRQOFNATTI 780  
Oy 781 PENDLEKTPMFAHHTPMKQVNSSDMLLROSPPHLSISDQAEKTYTFDDPS 840  
Db 781 PENDLEKTPMFAHHTPMKQVNSSDMLLROSPPHLSISDQAEKTYTFDDPS 840  
Oy 841 PGALDSNNSLSMTHFRRPOLHSGDVFPPESGLQLRNEKLGTTAATELKIDFVYST 900  
Db 841 PGALDSNNSLSMTHFRRPOLHSGDVFPPESGLQLRNEKLGTTAATELKIDFVYST 900



Qy	901	SNLITSTIPSDNIAAGTDNTSSLGAPSPMAYHDSDLTTLREKSSPLTSGEJPUSLEE	960
Dp	900	SNLITSTIPSDNIAAGTDNTSSLGAPSPMAYHDSDLTTLREKSSPLTSGEJPUSLEE	959
Qy	961	NMDSKLTLESGJLMSOESSMCKWVSTSGSLFGKFAHAPALTRKDNALFKVYSILTKTN	1020
Dp	960	NMDSKLTLESGJLMSOESSMCKWVSTSGSLFGKFAHAPALTRKDNALFKVYSILTKTN	1019
Qy	1021	KTSNNSATNKRTHIDPESLLIENSPWQIILSDPEFKYAPLPHBRLMDKNALTL	1080
Dp	1020	KTSNNSATNKRTHIDPESLLIENSPWQIILSDPEFKYAPLPHBRLMDKNALTL	1079
Qy	1081	NHMSKTTSSKNHMYOQKKESGPPDQAPDMSFFKMLFLPESARMYORTBCKNSLNG	1140
Dp	1080	NHMSKTTSSKNHMYOQKKESGPPDQAPDMSFFKMLFLPESARMYORTBCKNSLNG	1139
Qy	1141	OGSPKOLVSLGPEKSEVGEONFLSEKKNVYVVGGEPTKVDGLKEVAPSSNHLFTNLND	1200
Dp	1140	OGSPKOLVSLGPEKSEVGEONFLSEKKNVYVVGGEPTKVDGLKEVAPSSNHLFTNLND	1199
Qy	1201	LHENNTHOEXKLOEIEIEKKEFLIOENVVLPOJHTYGTGNKMKLFLSTGRONVGSVD	1260
Dp	1200	LHENNTHOEXKLOEIEIEKKEFLIOENVVLPOJHTYGTGNKMKLFLSTGRONVGSVD	1259
Qy	1261	GAYAPVLODPRSLNDSTNKTHTAHNSKKGEEENLEGLGNTOYIYEKACTTRISPT	1320
Dp	1260	GAYAPVLODPRSLNDSTNKTHTAHNSKKGEEENLEGLGNTOYIYEKACTTRISPT	1319
Qy	1321	SOONFVTOXRKRALKOPFLPEETLEKRIIVDTJSTOMSKMKHLPESTLTOIDYNEKE	1380
Dp	1320	SOONFVTOXRKRALKOPFLPEETLEKRIIVDTJSTOMSKMKHLPESTLTOIDYNEKE	1379
Qy	1381	KCAITQOSPLSCOTLRSHSIPQANRSPFLIAKVSFSPISPIYLTVLEFQONDSHLEPAAY	1440
Dp	1380	KCAITQOSPLSCOTLRSHSIPQANRSPFLIAKVSFSPISPIYLTVLEFQONDSHLEPAAY	1439
Qy	1441	RKSDGVOESHFLQAKKNNLSLAILTEMTGDQREVSJGTSKNTSVYTKKVEYNTVP	1500
Dp	1440	RKSDGVOESHFLQAKKNNLSLAILTEMTGDQREVSJGTSKNTSVYTKKVEYNTVP	1499
Qy	1501	KPDLPKTSIGVYELLPRVHYIYOKOLFPIETYSNGSPGHLDIYBSGLJQTEGAIKMEANRP	1560
Dp	1500	KPDLPKTSIGVYELLPRVHYIYOKOLFPIETYSNGSPGHLDIYBSGLJQTEGAIKMEANRP	1559
Qy	1561	GVPEPLRYAVAESSAKTPSKLDPJLAMDNHVQTOIPEEKMSOEKSPEKTAFFKDKDITLSL	1620
Dp	1560	GVPEPLRYAVAESSAKTPSKLDPJLAMDNHVQTOIPEEKMSOEKSPEKTAFFKDKDITLSL	1619
Qy	1621	NMCSNNAHIAINCGONKPEIEVYTAQOGPERLCSGNPVYLRHIOREITPTTLOSNOE	1680
Dp	1620	NMCSNNAHIAINCGONKPEIEVYTAQOGPERLCSGNPVYLRHIOREITPTTLOSNOE	1679
Qy	1681	IDYDOTTISVEKKKEDPIDYDEBENOSPPSFOKKTTHYFLAAVERLMDYGMSSPHYLRNR	1740
Dp	1680	IDYDOTTISVEKKKEDPIDYDEBENOSPPSFOKKTTHYFLAAVERLMDYGMSSPHYLRNR	1739
Qy	1741	AOSGSGVPOFKVYVOEFTDGSFTOLYVGELENIHGLGPLYIRAEVEDNIWYFRRQASR	1800
Dp	1740	AOSGSGVPOFKVYVOEFTDGSFTOLYVGELENIHGLGPLYIRAEVEDNIWYFRRQASR	1799
Qy	1801	PSFSFSLISIEEDOROGAEPKRNKVRKNEKTYFKMKVOYHMAHPKDEFDCAKAAFYSPV	1860
Dp	1800	PSFSFSLISIEEDOROGAEPKRNKVRKNEKTYFKMKVOYHMAHPKDEFDCAKAAFYSPV	1859
Qy	1861	DLEKRVHSGGLGPLYLCHNTLNPAAHGOYVQDFALFTITDEXKSMYFENNERRCRA	1920
Dp	1860	DLEKRVHSGGLGPLYLCHNTLNPAAHGOYVQDFALFTITDEXKSMYFENNERRCRA	1919
Qy	1921	PCNIOMEDPFEKENYREHAINGYIMDTLPGJLVAAODORIRMYLLMSGSENIHSHFSGH	1980
Dp	1920	PCNIOMEDPFEKENYREHAINGYIMDTLPGJLVAAODORIRMYLLMSGSENIHSHFSGH	1979

QY	1981	VPTAKKKEEKKALNYLNYGCFEYEMLPESKAGITMVECLIGELHLAGNSTLFLVYSSNK	2040
Db	1980	VPTAKKKEEKKALNYLYGVGEFVEMLPSKAGITMVECLIGELHLAGNSTLFLVYSSNK	2039
QY	2041	QTPGLMASGHIRDFOTTAAGCYGOMAPKRLRLHYSGSINAMSTKEPFSWIKYDLLAPMI	2100
Db	2040	QTPGLMASGHIRDFOTTAAGCYGOMAPKRLRLHYSGSINAMSTKEPFSWIKYDLLAPMI	2099
QY	2101	HKIKTQGRKQKFSLSYISOFITMYSLDGKMKQTYRGNSNGTLMVFEFGVNDSSGIKHNIFN	2160
Db	2100	HKIKTQGRKQKFSLSYISOFITMYSLDGKMKQTYRGNSNGTLMVFEFGVNDSSGIKHNIFN	2159
QY	2161	PIIARIYRLHPHYISIRSTLMELMGCDLNSCMP/LGMSKASISDQITASSYFTNNFA	2220
Db	2160	PIIARIYRLHPHYISIRSTLMELMGCDLNSCMP/LGMSKASISDQITASSYFTNNFA	2219
QY	2221	TWSPSKARHLQGRSNAMPQVNNPKEMLOVDFQKTMKVTGVTQGVKSLLTSMVYKEFL	2280
Db	2220	TWSPSKARHLQGRSNAMPQVNNPKEMLOVDFQKTMKVTGVTQGVKSLLTSMVYKEFL	2279
QY	2281	ISSSDQGHQMTLPEFGQKXKYVQGNQDSFTPVVNSLDP/LTR/LRHPQSWHOIATLRM	2340
Db	2280	ISSSDQGHQMTLPEFGQKXKYVQGNQDSFTPVVNSLDP/LTR/LRHPQSWHOIATLRM	2339
QY	2341	EVLGCEADLY 2351	
Db	2340	EVLGCEADLY 2350	
RESULT 96			
AA878223	ID	AA878223 standard; protein; 2351 AA.	
XX	AC	AA878223;	
XX	DT	15-NOV-1995 (first entry)	
XX	DE	Human Factor-VIII:c.	
XX	KN	Factor-VIII:c; blood-clotting; procoagulant; hemophilia;	
XX	KW	mutagenesis.	
OS	XX	Homo sapiens.	
PH	Key	Location/Qualifiers	
FT	Peptide	1..19	
FT		/label= sig_peptide	
FT	Cleavage-site	245..246	
FT		355..356	
FT		/label= APC_cleavage_site	
FT		581..582	
FT		/label= APC_cleavage_site	
FT		717..719	
FT		/label= Factor_Xa_cleavage_site	
FT		759..760	
FT		/label= 90-kDa_cleavage_site	
FT		795..796	
FT		/label= 95-kDa_cleavage_site	
FT		1332..1333	
FT		/label= 115-kDa_cleavage_site	
FT		1667..1668	
FT		/label= 76-kDa_cleavage_site	
FT		1740..1741	
FT		/label= Factor_Xa_cleavage_site	
PN	XX	US5422260-A.	
XX	PD	06-JUN-1995.	
XX	PF	29-MAY-1986.	86US-0868410.
XX	PR	02-DEC-1988.	88US-0279485.
XX	PR	29-MAY-1986.	86US-0868410.

PR 18-NOV-1986; 86US-0932767.  
PR 09-DEC-1986; 86US-093658.  
PR 15-MAY-1992; 92US-088936.  
XX  
XX (GEMV ) GENETICS INST INC.  
XX  
XX Kaufman RJ, Pittman DD, Tooole JJ;  
XX  
XX WPI, 1995-214657/28.  
XX  
XX New human factor VIII:c mutein(s) - useful for treating or preventing  
XX bleeding disorders  
XX  
XX  
XX Disclosure; Fig.1; 16pp; English.  
XX  
XX  
XX The sequence of natural human Factor-VIII:c is given in AAR78223.  
XX Mutagenesis of cDNA encoding the protein, resulting in deletion  
XX or substn. of key amino acid residues, allows produ. of Factor-  
XX VIII:c muteins with reduced lability for protease-catalyzed  
XX cleavage but with retained procoagulant activity.  
XX  
XX  
XX Sequence 2351 AA:  
Query Match 99.8%; Score 12396; DB 16; Length 2351;  
Best Local Similarity 99.9%; Pred. No. 0;  
Matches 2348; Conservative 1; Mismatches 2; Indels 0; Gaps 0;  
QY 1 MOTELSTCEFFCLLRFCFSATRRYYLGAVALSMQSDGLGELPDARFPFRVPSPPFN 60  
DB 1 MOTELSTCEFFCLLRFCFSATRRYYLGAVALSMQSDGLGELPDARFPFRVPSPPFN 60  
QY 61 TSVYKKTLFVEFTDHLNIAKPRPPWGLGPTIOAEYVDVVTIKNMASSHVSLHAY 120  
DB 61 TSVYKKTLFVEFTDHLNIAKPRPPWGLGPTIOAEYVDVVTIKNMASSHVSLHAY 120  
QY 121 GSVYWKASGAEYDDOTSQREKEDDKYFPGSHTYWOVLKENGPMASDPCLITYSYLSH 180  
DB 121 GSVYWKASGAEYDDOTSQREKEDDKYFPGSHTYWOVLKENGPMASDPCLITYSYLSH 180  
QY 181 VDLVKDNLNGLIGALLVCEGSLAKETKOTLHFTLLFVPEBGKSMHSETKNSLMODRD 240  
DB 181 VDLVKDNLNGLIGALLVCEGSLAKETKOTLHFTLLFVPEBGKSMHSETKNSLMODRD 240  
QY 241 AASARAMPKMHVYGVNRSPLGLIGCHRSKVYWHVIGMGTPEVHSIFLEBHTFLVYRNH 300  
DB 241 AASARAMPKMHVYGVNRSPLGLIGCHRSKVYWHVIGMGTPEVHSIFLEBHTFLVYRNH 300  
QY 301 ROASLEISPTTLELAOTLLMDLGOFLFCHTSSHOHGMFAVYKVDSCPEEPOLRMKNNE 360  
DB 301 ROASLEISPTTLELAOTLLMDLGOFLFCHTSSHOHGMFAVYKVDSCPEEPOLRMKNNE 360  
QY 361 EAEDYDDDLTDSMDVYFRDDNDSPTQIRSVAKKHKTWVHYIAEEDMDVAPLVLA 420  
DB 361 EAEDYDDDLTDSMDVYFRDDNDSPTQIRSVAKKHKTWVHYIAEEDMDVAPLVLA 420  
QY 421 PDDRSYKSOYLNNNGPORIGRKYKVRMAAYTDEFKTRREALIOHESGILLPILLYGVGDTL 480  
DB 421 PDDRSYKSOYLNNNGPORIGRKYKVRMAAYTDEFKTRREALIOHESGILLPILLYGVGDTL 480  
QY 481 LIIFKNQASRPYNYTHGHITDVPRPLYSRRLPKGVKHLKDPILLPGEIFYKKTIVVEGSP 540  
DB 481 LIIFKNQASRPYNYTHGHITDVPRPLYSRRLPKGVKHLKDPILLPGEIFYKKTIVVEGSP 540  
QY 541 TKSDPRCLTRYSSPFVNMERDLASGLIPLLICKESSVDQRGNQIMSDRNVILFVDE 600  
DB 541 TKSDPRCLTRYSSPFVNMERDLASGLIPLLICKESSVDQRGNQIMSDRNVILFVDE 600  
QY 601 NRSWTLTENIORLPNPAGVQLEDEPQASNMHMSINGYVPSLSQSVCLHVAAYWYLLS 660  
DB 601 NRSWTLTENIORLPNPAGVQLEDEPQASNMHMSINGYVPSLSQSVCLHVAAYWYLLS 660  
QY 661 IGAOTDFLSVFFSGYTFKHKMYEDTLTLFPFSGETVFMSENPGLMILGCHNSDFRNG 720  
DB 661 IGAOTDFLSVFFSGYTFKHKMYEDTLTLFPFSGETVFMSENPGLMILGCHNSDFRNG 720

DB 661 IGAOTDFLSVFFSGYTFKHKMYEDTLTLFPFSGETVFMSENPGLMILGCHNSDFRNG 720  
QY 721 MTALLKVSQCDKNTGDIYEDYEDISAVLLSKNNALIEPFSQNSRHPSTROKQFNATTI 780  
DB 721 MTALLKVSQCDKNTGDIYEDYEDISAVLLSKNNALIEPFSQNSRHPSTROKQFNATTI 780  
QY 781 PENDIEKTDWFAHRTPMKIONVSSSDLLMLKQSTPRGSLSDLOAKETESDDPS 840  
DB 781 PENDIEKTDWFAHRTPMKIONVSSSDLLMLKQSTPRGSLSDLOAKETESDDPS 840  
QY 841 PGALIDNNLSSEMTHERPOLHSGDMVTFPESGLQRLNEKLTCTAATPKLDPKVSST 900  
DB 841 PGALIDNNLSSEMTHERPOLHSGDMVTFPESGLQRLNEKLTCTAATPKLDPKVSST 900  
QY 901 SNNLITPTSDNLAAAGDMTSSLGPPSPVHYDSOLDTTLFGKSSPLTESGSPLSSEE 960  
DB 901 SNNLITPTSDNLAAAGDMTSSLGPPSPVHYDSOLDTTLFGKSSPLTESGSPLSSEE 960  
QY 961 NNDKSLIESGLMNSQESSWGKNVSTESGRLEPKRAHGPALLTKDNALFKVSI SLKTN 1020  
DB 961 NNDKSLIESGLMNSQESSWGKNVSTESGRLEPKRAHGPALLTKDNALFKVSI SLKTN 1020  
QY 1021 KTSNNSATNRKTHIDGPSLTIENSQSVNQNLIESDTEFEKKVTPFLIDRMADKNATLRL 1080  
DB 1021 KTSNNSATNRKTHIDGPSLTIENSQSVNQNLIESDTEFEKKVTPFLIDRMADKNATLRL 1080  
QY 1081 NMSKNTTSSKNMEMVOQKEGPIPPDAQNPDMSFPFKMLFLPSASVIOIRGKNSLNSG 1140  
DB 1081 NMSKNTTSSKNMEMVOQKEGPIPPDAQNPDMSFPFKMLFLPSASVIOIRGKNSLNSG 1140  
QY 1141 QGSPSKQVLSLGPESKSVESQNFLESEKNKVVYKGGEFTKDVGLEBMVFPSSRLFTLNIDN 1200  
DB 1141 QGSPSKQVLSLGPESKSVESQNFLESEKNKVVYKGGEFTKDVGLEBMVFPSSRLFTLNIDN 1200  
QY 1201 LHENNTHOEKKIOEELIEKKEITLIONNVLPQIRHVYCTKFKMKNLFLSTRONVGSGY 1260  
DB 1201 LHENNTHOEKKIOEELIEKKEITLIONNVLPQIRHVYCTKFKMKNLFLSTRONVGSGY 1260  
QY 1261 GAVAPYLODFRSLDSTNRKTKHTAFHSKKEEENLESLQKOTQIYEXACTRISPT 1320  
DB 1261 GAVAPYLODFRSLDSTNRKTKHTAFHSKKEEENLESLQKOTQIYEXACTRISPT 1320  
QY 1321 SOONVYTORSKRALKOPRLPLEETLEKRTIYDDPSTOWSKNMKHLPTSLQIDYNEKE 1380  
DB 1321 SOONVYTORSKRALKOPRLPLEETLEKRTIYDDPSTOWSKNMKHLPTSLQIDYNEKE 1380  
QY 1381 KGATQSPSLDCLTRSHSIPQANRSPPLAKVSSPSTIRPYLTRVLFQONSHTLPASV 1440  
DB 1381 KGATQSPSLDCLTRSHSIPQANRSPPLAKVSSPSTIRPYLTRVLFQONSHTLPASV 1440  
QY 1441 RKDQSGVQESSHFTLOGAKKNNLSLAILTEMTGDDREVGSIGTSATNSVYKKVENVYLP 1500  
DB 1441 RKDQSGVQESSHFTLOGAKKNNLSLAILTEMTGDDREVGSIGTSATNSVYKKVENVYLP 1500  
QY 1501 KPDLPTSGKVELLPKHVITOKDLPLETNSGSPGHLDLVGSGLSOCTBEATIKWNAANRP 1560  
DB 1501 KPDLPTSGKVELLPKHVITOKDLPLETNSGSPGHLDLVGSGLSOCTBEATIKWNAANRP 1560  
QY 1561 GKVPFLRVATESACTPESKLLPLANDNHGTOIPKEEMKSOEKSPEKTAFFKKDITLSL 1620  
DB 1561 GKVPFLRVATESACTPESKLLPLANDNHGTOIPKEEMKSOEKSPEKTAFFKKDITLSL 1620  
QY 1621 NACESNHAIAAINEQONKPELEIYMAKOGTELTSONPVYLAHROREIRRTLOSQOE 1680  
DB 1621 NACESNHAIAAINEQONKPELEIYMAKOGTELTSONPVYLAHROREIRRTLOSQOE 1680  
QY 1681 IDVDPTISYEMKKEEDFDIYDENQSPRSFOKKTTRHYTAVERLMDYGSSSPHYLRNR 1740  
DB 1681 IDVDPTISYEMKKEEDFDIYDENQSPRSFOKKTTRHYTAVERLMDYGSSSPHYLRNR 1740  
QY 1741 AOGSGVPOKRVVPOEFTDGSFTQPLRGELNHLGLGLPRTYRAVEDNIMWVFRNQASR 1800  
DB 1741 AOGSGVPOKRVVPOEFTDGSFTQPLRGELNHLGLGLPRTYRAVEDNIMWVFRNQASR 1800

QY 1801 PYSFYSLLSYEEDROGAREPRKNTKTYEMKVOHHMAPTKDEPDCKAAAYSDV 1860  
DB 1801 PYSFYSLLSYEEDROGAREPRKNTKTYEMKVOHHMAPTKDEPDCKAAAYSDV 1860  
QY 1861 DLEKDVHSGILGILLVCHNTLPAHQVQVQEFALFTIEDETKSWYFTEENMRNCR 1920  
DB 1861 DLEKDVHSGILGILLVCHNTLPAHQVQVQEFALFTIEDETKSWYFTEENMRNCR 1920  
QY 1921 PCNIQMEDPTFKENYRPHAINGYINDTLPGLVMAQDORIRMYLLSGNSENHSHFSGH 1980  
DB 1921 PCNIQMEDPTFKENYRPHAINGYINDTLPGLVMAQDORIRMYLLSGNSENHSHFSGH 1980  
QY 1981 VETVRKKEEYKALYXNYPGVFEVYEMLPKSKAGIMRVECLIGHLHAGSTLFLYYSKC 2040  
DB 1981 VETVRKKEEYKALYXNYPGVFEVYEMLPKSKAGIMRVECLIGHLHAGSTLFLYYSKC 2040  
QY 2041 QTPPLGMAHGIRDFQITASGOYQWAPKLARLHSGSINAMSTKEPFSMIKVDLLAPMI 2100  
DB 2041 QTPPLGMAHGIRDFQITASGOYQWAPKLARLHSGSINAMSTKEPFSMIKVDLLAPMI 2100  
QY 2101 HGIKTOGAROKFSSLYISOFITIMYSLDGKKMQTYRGANSTGTLWVFFGANDSSGIKHNIFN 2160  
DB 2101 HGIKTOGAROKFSSLYISOFITIMYSLDGKKMQTYRGANSTGTLWVFFGANDSSGIKHNIFN 2160  
QY 2161 PPIIARVIRLPHPTHTYSTRSLRMEIMCDLNSCMPLGMSKATISNOITASSYPTNMEA 2220  
DB 2161 PPIIARVIRLPHPTHTYSTRSLRMEIMCDLNSCMPLGMSKATISNOITASSYPTNMEA 2220  
QY 2221 TWSPSKARLHQGRSNMARPQVNNKPEMLQVDFQKTKMYGVTVTQGVKSILTSMYKPEL 2280  
DB 2221 TWSPSKARLHQGRSNMARPQVNNKPEMLQVDFQKTKMYGVTVTQGVKSILTSMYKPEL 2280  
QY 2281 ISSSDQGHQWTLFQNGKVKVFOGNDSTFPVNSLDPPLTTRYLRIHQSWVHQAIALRM 2340  
DB 2281 ISSSDQGHQWTLFQNGKVKVFOGNDSTFPVNSLDPPLTTRYLRIHQSWVHQAIALRM 2340  
QY 2341 EVLGCPEADLY 2351  
DB 2341 EVLGCPEADLY 2351

RESULT 97  
AAW11460  
ID AAW11460 standard; Protein: 2349 AA.  
AC AAW11460;  
XX  
DT 20-NOV-1997 (first entry)  
XX  
DE Active Factor VIII:C analogue residue 1716, 1717 deletion.  
XX  
KW Factor VIII:C; analogue: glycoprotein; blood coagulation cascade;  
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;  
KW plasma protease; thrombin; immunogen; antibody; haemophilic; therapy;  
XX  
OS Homo sapiens.  
OS Synthetic.  
FH  
FH Key Location/Qualifiers  
FT Peptide 1..19  
FT Protein /note= "signal peptide"  
FT /note= "mature Factor VIII:C"  
FT Region 20..2349  
FT /note= "heavy chain fragment"  
FT Region 1668..2348  
FT /note= "light chain fragment"  
FT Domain 760..1667  
FT /note= "B domain"  
FT Misc-difference 1734..1735  
FT /note= "site of 2 residue deletion"

XX  
PN M09703195-A1.  
XX  
PD 30-JAN-1997.  
XX  
PF 09-JUL-1996; 96WO-0511444.  
XX  
PR 11-JUL-1995; 95US-0001025.  
XX  
PA (CHIR ) CHIRON CORP.  
PI Cohen FE, Hung DT, Innis M;  
XX  
DR WPI; 1997-119050/11.  
XX  
PF Factor VIII:C analog modified adjacent to a non-activating Arg  
PT residue - used in the treatment of haemophilias, by improvement of  
PS haemostasis  
XX  
XX Claim 36; Page -; 90pp; English.  
XX  
CC AAW1330-W11472 represent active Factor VIII:C analogues of the  
CC invention. These sequences were created by mutating the wild type Factor  
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The  
CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC peptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC X-chromosome-linked inherited bleeding diathesis, Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophilias, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.  
XX  
SQ Sequence 2349 AA;  
Query Match 99.8%; Score 12395; DB 18; Length 2349;  
Best Local Similarity 99.9%; Pred. No. 0;  
Matches 2349; Conservative 0; Mismatches 0; Indels 2; Gaps 1;  
QY 1 MOTELSTCEPFLCLARFCFSATRRYYLGAIVELSMOYMSDGLPVDARPPRPVPSPPFN 60  
DB 1 MOTELSTCEPFLCLARFCFSATRRYYLGAIVELSMOYMSDGLPVDARPPRPVPSPPFN 60  
QY 61 TSVYIKKTLVEYETDHLFNIARPPRMGLCAPTIOAEVYDYVITLKKMASHPVSLHAV 120  
DB 61 TSVYIKKTLVEYETDHLFNIARPPRMGLCAPTIOAEVYDYVITLKKMASHPVSLHAV 120  
QY 121 GVSVMKASGAEYDDQTSOREKEDDKVFPFGSHYVWQVLKENGPMASDPLCLTYSLSH 180  
DB 121 GVSVMKASGAEYDDQTSOREKEDDKVFPFGSHYVWQVLKENGPMASDPLCLTYSLSH 180  
QY 181 VDIYMDLNSGLIGALVCRGSGLAKERTOTLTKFTLLFAVDEGKSMHSEPTKNSLMORD 240  
DB 181 VDIYMDLNSGLIGALVCRGSGLAKERTOTLTKFTLLFAVDEGKSMHSEPTKNSLMORD 240  
QY 241 AASARAMPKMTVNGVYNSRLPGLICCHRSYVWVHVGMTGTEPVHSITLSEHTFLVNNH 300  
DB 241 AASARAMPKMTVNGVYNSRLPGLICCHRSYVWVHVGMTGTEPVHSITLSEHTFLVNNH 300  
QY 301 RQNSIRKSLTFLTAQTLAMDLOFLFLFCHISSHODGMEAYVVDSCPEPOLMKKNE 360  
DB 301 RQNSIRKSLTFLTAQTLAMDLOFLFLFCHISSHODGMEAYVVDSCPEPOLMKKNE 360  
QY 361 EADYDDDLTDSNDVYRFPDDNSPSFIDIRSVAKKHRTVNHIAABEDMDVAPLVLA 420

|||||  
Db 361 EAEDYDDDLTDESEMDVYRFDDDDSPSFIQIRSAVKAKKPKTWVHYIAAEEDMDVAPLVLA 420  
Oy 421 PDDRSYKSOYLNNNGPOIGKRYKYKVRMAVYNDDEFKTRERAIQHESGTIGPLLXGCVDTL 480  
Db 421 PDDRSYKSOYLNNNGPOIGKRYKYKVRMAVYNDDEFKTRERAIQHESGTIGPLLXGCVDTL 480  
Oy 481 LIIFKNOASRPYNYIPHGITDVAPLYSRRLPKGVKHLKDFPILPGEIFKWTVTVEDGP 540  
Db 481 LIIFKNOASRPYNYIPHGITDVAPLYSRRLPKGVKHLKDFPILPGEIFKWTVTVEDGP 540  
Oy 541 TKSDPRCLTRYSSSFVMMERDLASGLIGPLLICKEVSVDORGNOQMSDRNVLTFESVE 600  
Db 541 TKSDPRCLTRYSSSFVMMERDLASGLIGPLLICKEVSVDORGNOQMSDRNVLTFESVE 600  
Oy 601 NRSWLTENIORFLPNPAGVQLEDEPFQASNMHSHINGVFDLSQVGLHFAVAYWYLLS 660  
Db 601 NRSWLTENIORFLPNPAGVQLEDEPFQASNMHSHINGVFDLSQVGLHFAVAYWYLLS 660  
Oy 661 IGAQDFLSVFFSGYTFKHKMYEDTLPLPPSGEIVFMSMENPGLMILGCHNSDFRNG 720  
Db 661 IGAQDFLSVFFSGYTFKHKMYEDTLPLPPSGEIVFMSMENPGLMILGCHNSDFRNG 720  
Oy 721 MTALLKVSQCDKNFGDYEDSYEDISAYLLSKNNAIEPRFSQNSRHPSTRQKOPNATTI 780  
Db 721 MTALLKVSQCDKNFGDYEDSYEDISAYLLSKNNAIEPRFSQNSRHPSTRQKOPNATTI 780  
Oy 781 PENDIEKTDPRFAHRTPMKTIQWSSDLMILNQSPTPHGILSLSLQAKETFSDDPS 840  
Db 781 PENDIEKTDPRFAHRTPMKTIQWSSDLMILNQSPTPHGILSLSLQAKETFSDDPS 840  
Oy 841 PGALDSNNLSLEMTHEFPOLHNSGDMVFTPEBSGQOLRLNEKLGTTATATELKLDFKYST 900  
Db 841 PGALDSNNLSLEMTHEFPOLHNSGDMVFTPEBSGQOLRLNEKLGTTATATELKLDFKYST 900  
Oy 901 SNNLISTIPSDNLAAQDNTSSLGPPSMVHYDSOLDTLTFGKSSPLTESGPPSLSEE 960  
Db 901 SNNLISTIPSDNLAAQDNTSSLGPPSMVHYDSOLDTLTFGKSSPLTESGPPSLSEE 960  
Oy 961 NNDKLLSGLMNSOESMGKNYSSTESGRLEFKRAHGPALLTKRNALFKVSTISLKTN 1020  
Db 961 NNDKLLSGLMNSOESMGKNYSSTESGRLEFKRAHGPALLTKRNALFKVSTISLKTN 1020  
Oy 1021 KTSNNSATNRKTHIDGFSLLIENSPSVWONILIESDTEFKKVTPLIDHRLMDKNATLRL 1080  
Db 1021 KTSNNSATNRKTHIDGFSLLIENSPSVWONILIESDTEFKKVTPLIDHRLMDKNATLRL 1080  
Oy 1081 NHMSNKTTSKKNMEMVOQKKEGPIPPDAQNPDMSEFKMLFLPESARMIQRTGKNSLNSG 1140  
Db 1081 NHMSNKTTSKKNMEMVOQKKEGPIPPDAQNPDMSEFKMLFLPESARMIQRTGKNSLNSG 1140  
Oy 1141 OGSPKOLVSLGPEKSYEGONFLSEKNKYVVGKEPTKDVGLKEMVFPSSRNLFTNTDN 1200  
Db 1141 OGSPKOLVSLGPEKSYEGONFLSEKNKYVVGKEPTKDVGLKEMVFPSSRNLFTNTDN 1200  
Oy 1201 LHENNTHNQERKIOEELIEKRETLIOENVVLPOIHTVTGKNFKNLFLLSTRONVGSYD 1260  
Db 1201 LHENNTHNQERKIOEELIEKRETLIOENVVLPOIHTVTGKNFKNLFLLSTRONVGSYD 1260  
Oy 1261 GAYAPVLQDFRSLNDSTNRTKHTAHFASKGGEENLGLGNQTKOIVEYACTTRISNT 1320  
Db 1261 GAYAPVLQDFRSLNDSTNRTKHTAHFASKGGEENLGLGNQTKOIVEYACTTRISNT 1320  
Oy 1321 SOONFVTOBSKRALKQRLPLETELEKRIYDVTSTOWSKNNKHLTPSTLQIDYNSKE 1380  
Db 1321 SOONFVTOBSKRALKQRLPLETELEKRIYDVTSTOWSKNNKHLTPSTLQIDYNSKE 1380  
Oy 1381 KGATQSPPLSDCLTRSHSIPQANRSEPLAKVSSPSPRIPLYLTVLPQDNSHLPASY 1440  
Db 1381 KGATQSPPLSDCLTRSHSIPQANRSEPLAKVSSPSPRIPLYLTVLPQDNSHLPASY 1440  
Oy 1441 RKDSGVOESSHFIQAKKKNLSLALITLMTGQREVSLGTSATNSYTKKAVNTYLP 1500  
Db 1441 RKDSGVOESSHFIQAKKKNLSLALITLMTGQREVSLGTSATNSYTKKAVNTYLP 1500

Db 1441 RKDSGVOESSHFIQAKKKNLSLALITLMTGQREVSLGTSATNSYTKKAVNTYLP 1500  
Oy 1501 KPDLPKTSQKVELLPVYHIYOKDLPTETSNCSGHLDIYESGLQTEGAIKKNENRNP 1560  
Db 1501 KPDLPKTSQKVELLPVYHIYOKDLPTETSNCSGHLDIYESGLQTEGAIKKNENRNP 1560  
Oy 1561 GVPPLRYATESSAKTPSKLDPPLANDHNYGTQIPKEEMKSQEKSEPTAKKQDTLLS 1620  
Db 1561 GVPPLRYATESSAKTPSKLDPPLANDHNYGTQIPKEEMKSQEKSEPTAKKQDTLLS 1620  
Oy 1621 NACESNHAIAINEGQNKPEIEYTWAKGRTERYCSQNPVLRKHOREITRTTLOSQOE 1680  
Db 1621 NACESNHAIAINEGQNKPEIEYTWAKGRTERYCSQNPVLRKHOREITRTTLOSQOE 1680  
Oy 1681 IDYDPTISVEKKKEDDIYDEBENSPPRSPOKTRHYFLAAVERLMDYGSSPHVLRNR 1740  
Db 1681 IDYDPTISVEKKKEDDIYDEBENSPPRSPOKTRHYFLAAVERLMDYGSSPHVLRNR 1740  
Oy 1741 AOSGSVPQFKKVFQEFTHGSGFTQPLYNGEI.NEHLGLPFIYAEYEDNIMVTRNOASR 1800  
Db 1741 AOSGSVPQFKKVFQEFTHGSGFTQPLYNGEI.NEHLGLPFIYAEYEDNIMVTRNOASR 1800  
Oy 1801 PYSFYSLSIYEEDORQGAEPKKNFVKNENETKTYFMKVQHNAAPTRKDEPDKAANAPESDV 1860  
Db 1801 PYSFYSLSIYEEDORQGAEPKKNFVKNENETKTYFMKVQHNAAPTRKDEPDKAANAPESDV 1860  
Oy 1861 DLEKDVHSGTIGPLVCHNTLNTPAHGROVTVQBFALFTIPDETSMYFTENNERCRA 1920  
Db 1861 DLEKDVHSGTIGPLVCHNTLNTPAHGROVTVQBFALFTIPDETSMYFTENNERCRA 1920  
Oy 1921 PCNIOMEDPTFKENYRPHAINGYIMDTPLGLVMAQDRIWYLLSGNSNENHSHIFSGH 1980  
Db 1921 PCNIOMEDPTFKENYRPHAINGYIMDTPLGLVMAQDRIWYLLSGNSNENHSHIFSGH 1980  
Oy 1981 VFTYRKKEEYKEMALYNLYGVEFEVEMLPKRAKGIWRECLIGENHLHAGSTLFLVSNKC 2040  
Db 1981 VFTYRKKEEYKEMALYNLYGVEFEVEMLPKRAKGIWRECLIGENHLHAGSTLFLVSNKC 2040  
Oy 2041 QPTLGMASGHTRDQITZASGOYQOMAPLALHYSGSINMSKKEPFSKIVDILAMIT 2100  
Db 2041 QPTLGMASGHTRDQITZASGOYQOMAPLALHYSGSINMSKKEPFSKIVDILAMIT 2100  
Oy 2101 HGIKTQARQKFESSLYISQFIITMYSLDGKKWQYRNGSTGTLMVFFGNVDSGIRKHIFN 2160  
Db 2101 HGIKTQARQKFESSLYISQFIITMYSLDGKKWQYRNGSTGTLMVFFGNVDSGIRKHIFN 2160  
Oy 2159 PPIIARYIRLHPHYSTIRSLRMEIMCGDLNCSMPLGMSKASIDAOITTASVYTNMFA 2218  
Db 2159 PPIIARYIRLHPHYSTIRSLRMEIMCGDLNCSMPLGMSKASIDAOITTASVYTNMFA 2218  
Oy 2221 TWSPSKARLHLOGSNAMRPOVNNPKEMLOVDPOKTKMYGVGTQGVSLTSMYKREFL 2280  
Db 2221 TWSPSKARLHLOGSNAMRPOVNNPKEMLOVDPOKTKMYGVGTQGVSLTSMYKREFL 2280  
Oy 2281 ISSSODGHQWTLFQNGKYKVTQGNDSFTPVNSLDPLLRYLRIHPQSWHQAALRM 2340  
Db 2281 ISSSODGHQWTLFQNGKYKVTQGNDSFTPVNSLDPLLRYLRIHPQSWHQAALRM 2340  
Oy 2341 EYLGCBAQDLY 2351  
Db 2341 EYLGCBAQDLY 2349

RESULT 98  
AAK5352  
ID AAK5352 standard; Protein; 2351 AA.  
AAK5352;  
10-NOV-1994 (first entry)  
Sequence of human factor VIII.

KW Factor VIII: haemostasis; haemophilia A; clotting cascade;  
KM fibrinogen; fibrin; thrombin; proteolytic enzyme; co-factor.  
XX  
OS Homo sapiens.  
XX  
PN M09411503-A.  
XX  
PD 26-MAY-1994.  
XX  
PF 01-OCT-1993; 93WO-US09438.  
XX  
PR 13-NOV-1992; 92US-0976086.  
PR 14-SEP-1993; 93US-0121202.  
XX  
PA (GEMT ) GENETICS INST INC.  
XX  
PI Kaufman RJ, Pittman D, Rehemtulla A, Wozney JM;  
XX  
XX WPI: 1994-183504/22.  
DR N-PSDB; AA066615.  
XX  
XX Nucleic acid encoding porcine factor VIII - used to obtain  
PT porcine and human-porcine chimeric factor VIII for treating  
PT haemophilia  
PS  
PS Disclosure: Page 27-36; 61pp; English.  
XX  
XX Prepn. of human factor VIII cDNA has been set forth in detail, e.g.,  
CC US Patent No. 4,757,006 issued July 12, 1988 and in Toole et al.,  
CC Nature 312:312(1984). A recombinant clone contg. the nucleotide  
CC sequence in AA066615, designated as pSP64-VIII, is on deposit at the  
CC ATCC under Accession No. ATCC 39812. Chimeric forms of factor VIII  
CC include those where various domains of the human factor VIII have  
CC been replaced, in whole or in part, by analogous porcine factor VIII  
CC domains, and include, chimeric forms where the A1 and/or A2 domains,  
CC in whole or in part, of the human factor VIII sequence have been  
CC replaced, in whole or in part, by the A1 and/or the A2 domains of  
CC porcine factor VIII. Specifically provided are chimeric factor VIII  
CC sequences comprising the A1, A2, A3, B, C1 and C2 human domains as  
CC set forth in AA066615, where the A1 and/or A2 domains, as well as  
CC other segments, such as the regions corresp. to the AA numbers  
CC 336-372, 336-740, 372-740, 700-740 and combinations of these  
CC regions have been replaced in whole or in part with porcine factor  
CC VIII sequences as set forth in AA066616 and AAR55353.  
XX  
XX Sequence 2351 AA:  
SQ

Query Match 99.8%; Score 12395; DB 15; Length 2351;  
Best Local Similarity 99.9%; Pred. No. 0;  
Matches 2348; Conservative 1; Mismatches 2; Indels 0; Gaps 0;

QY 1 MOELSTCFPLCLLRFCFSATRRYYLGAVELSMQSDGLGELPVARPPVPKSPFFN 60  
DB 1 MOELSTCFPLCLLRFCFSATRRYYLGAVELSMQSDGLGELPVARPPVPKSPFFN 60  
QY 61 TSVYKKKTLFEFTDHLFNIAKRPMMGILLPTIOAEVYDVIYTLKMAHPSLHAY 120  
DB 61 TSVYKKKTLFEFTVHLFNIAKRPMMGILLPTIOAEVYDVIYTLKMAHPSLHAY 120  
QY 121 GVSYWKASGAEYDDQTSQREKEDKYFPGGSHTYVWQVLKENGPMASDPLCLTAYSLH 180  
DB 121 GVSYWKASGAEYDDQTSQREKEDKYFPGGSHTYVWQVLKENGPMASDPLCLTAYSLH 180  
QY 181 VDLVKDNLNSGLIGALVYREGSLAKERTQTLHKFTLLFVPEBGSMHSETRKNSLMODRD 240  
DB 181 VDLVKDNLNSGLIGALVYREGSLAKERTQTLHKFTLLFVPEBGSMHSETRKNSLMODRD 240  
QY 241 AASARAPKMHYVNGVNSRLPGLIGCHRSVYWHVIGMGTTPPEVHSIFLREGHTFLVNH 300  
DB 241 AASARAPKMHYVNGVNSRLPGLIGCHRSVYWHVIGMGTTPPEVHSIFLREGHTFLVNH 300  
QY 301 ROASLEISPTTFLTAOTLLMDLGOFLFCHSHSHODGMEAYVYKVDSCPEEQLRMKNE 360  
DB 301 ROASLEISPTTFLTAOTLLMDLGOFLFCHSHSHODGMEAYVYKVDSCPEEQLRMKNE 360

DB 301 ROASLEISPTTFLTAOTLLMDLGOFLFCHSHSHODGMEAYVYKVDSCPEEQLRMKNE 360  
QY 361 EAEDYDDLTDSEMDVVRDDNDSPSFQIINSVAKKHPTWVHYIAEEBEDVYAPLVIA 420  
DB 361 EAEDYDDLTDSEMDVVRDDNDSPSFQIINSVAKKHPTWVHYIAEEBEDVYAPLVIA 420  
QY 421 PDDRSYKSOYLLNNGPQIRGKKYKRFMAAYDEFEKREAIQIHESGILGPILYGEGVDTL 480  
DB 421 PDDRSYKSOYLLNNGPQIRGKKYKRFMAAYDEFEKREAIQIHESGILGPILYGEGVDTL 480  
QY 481 LIIFKNQASRPYNIYHGTIDVRLPYLSRRLPKGVKHLKEPILPGEIFRYKWTYVEDGP 540  
DB 481 LIIFKNQASRPYNIYHGTIDVRLPYLSRRLPKGVKHLKEPILPGEIFRYKWTYVEDGP 540  
QY 541 TKSDPCLTRYSSPFVNMERDLASGLIGPILICVKESVQROGNOIMSKRNVITLPSVDE 600  
DB 541 TKSDPCLTRYSSPFVNMERDLASGLIGPILICVKESVQROGNOIMSKRNVITLPSVDE 600  
QY 601 NRSWYLTENIQRFPLNPAGVLEDEFEQASNIMHSINGYVFDLQSVCLHEVAYWYLS 660  
DB 601 NRSWYLTENIQRFPLNPAGVLEDEFEQASNIMHSINGYVFDLQSVCLHEVAYWYLS 660  
QY 661 IGAOTDFLSVFEFGYTFKHKWYEDTTLTPPESGETVYFMSMENPGLMILGCHNSDPFRNG 720  
DB 661 IGAOTDFLSVFEFGYTFKHKWYEDTTLTPPESGETVYFMSMENPGLMILGCHNSDPFRNG 720  
QY 721 MTALLKVSCKDKNQDGYEDYEDISAYLLSKNNAIEPFSQNSRHPSTROKOFNAATTI 780  
DB 721 MTALLKVSCKDKNQDGYEDYEDISAYLLSKNNAIEPFSQNSRHPSTROKOFNAATTI 780  
QY 781 PENDIEKTPWFHRTPMPIKQIONVSSDLMMLROSPFHGSLSDLOEAYVEFSDPS 840  
DB 781 PENDIEKTPWFHRTPMPIKQIONVSSDLMMLROSPFHGSLSDLOEAYVEFSDPS 840  
QY 841 PGALDSNLSLEKTHFRQLHSGDMVFPESGLQRLNEKLGTTAATELKKLDFKVSST 900  
DB 841 PGALDSNLSLEKTHFRQLHSGDMVFPESGLQRLNEKLGTTAATELKKLDFKVSST 900  
QY 901 SNNLSTIPSDNLAAGTNTSSILGPPSMAPHYQSODTTLTFKSKSSPTLSESGPLSSEE 960  
DB 901 SNNLSTIPSDNLAAGTNTSSILGPPSMAPHYQSODTTLTFKSKSSPTLSESGPLSSEE 960  
QY 961 NNSKILLEGILNNSOESSMGKVNSTSSGLRFGKRAHROPALLTDNALFKVYSISLLKTN 1020  
DB 961 NNSKILLEGILNNSOESSMGKVNSTSSGLRFGKRAHROPALLTDNALFKVYSISLLKTN 1020  
QY 1021 KTSNNSATNRKTHIDGPSLLIENSFVWQNILESDFEKKVPTLIHDRMLMDKNAATLRL 1080  
DB 1021 KTSNNSATNRKTHIDGPSLLIENSFVWQNILESDFEKKVPTLIHDRMLMDKNAATLRL 1080  
QY 1081 NHHNSKTTSSKMEVNOQKKEGPIPPDAONPDMSEPFKMLLPESAARVIORHGKNSLNSG 1140  
DB 1081 NHHNSKTTSSKMEVNOQKKEGPIPPDAONPDMSEPFKMLLPESAARVIORHGKNSLNSG 1140  
QY 1141 QGSPKQOLVSLGPEKSVBGNFLESKKVVVVGGEFTKDVGLKEAVPSSRNLLFTNLON 1200  
DB 1141 QGSPKQOLVSLGPEKSVBGNFLESKKVVVVGGEFTKDVGLKEAVPSSRNLLFTNLON 1200  
QY 1201 LHEENHNHNEKQIOEIEIKKFTLLQENNVLPQIHVYTGKNNKMLFLSLTRONVBSST 1260  
DB 1201 LHEENHNHNEKQIOEIEIKKFTLLQENNVLPQIHVYTGKNNKMLFLSLTRONVBSST 1260  
QY 1261 GAYAPVLODFNSLNDSTNRKTHAHFSKKGEEENLEGAGNTOQIOVEKYACTRTISPNT 1320  
DB 1261 GAYAPVLODFNSLNDSTNRKTHAHFSKKGEEENLEGAGNTOQIOVEKYACTRTISPNT 1320  
QY 1321 SQONFVTOQSKKALKQOPFLPLEETLEKRTIYVDNSTQSKMKMLPSTLTJOIDVNEKE 1380  
DB 1321 SQONFVTOQSKKALKQOPFLPLEETLEKRTIYVDNSTQSKMKMLPSTLTJOIDVNEKE 1380  
QY 1381 KGAITOSPISDCLTRSHSIRQANRSPPLAKVSSPSTIRPIYLTRVLFDONSSHLPAAST 1440  
DB 1381 KGAITOSPISDCLTRSHSIRQANRSPPLAKVSSPSTIRPIYLTRVLFDONSSHLPAAST 1440

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OY 1441 RKKDSGVQESSHFLQGAKKNNLSLAITLLEMTGDQREVSLGTSATNSVTYKKKVENTVLP 1500
    |||||||
Db 1441 RKKDSGVQESSHFLQGAKKNNLSLAITLLEMTGDQREVSLGTSATNSVTYKKKVENTVLP 1500
OY 1501 KPDLPTSGKVELLPKRVHLYQKDLPEPTETNSGSPGHLIDVESSLQGTGGAIKKNEANRP 1560
    |||||||
Db 1501 KPDLPTSGKVELLPKRVHLYQKDLPEPTETNSGSPGHLIDVESSLQGTGGAIKKNEANRP 1560
OY 1561 GKVPFLKVAATESAKTPSKLDPLAMDNHGYTOIPKEEMKSOEKSPKTAFFKKKDTLTL 1620
    |||||||
Db 1561 GKVPFLKVAATESAKTPSKLDPLAMDNHGYTOIPKEEMKSOEKSPKTAFFKKKDTLTL 1620
OY 1621 NACESNHAIAINEGONKPEIEVYMAQGRERLCSQNPVYKRRQRELTTRTTLQSQOE 1680
    |||||||
Db 1621 NACESNHAIAINEGONKPEIEVYMAQGRERLCSQNPVYKRRQRELTTRTTLQSQOE 1680
OY 1681 IDYDDTISYEMKKEDEPDIDEDENOSPRSFQKTRHVFIAAVERLMDYGMSSPHVLNR 1740
    |||||||
Db 1681 IDYDDTISYEMKKEDEPDIDEDENOSPRSFQKTRHVFIAAVERLMDYGMSSPHVLNR 1740
OY 1741 AOSGSVPQKKVYQOEFTDGSFTQPLVYKGLNEHLGLGPLYRAVEENIMVTRRQASR 1800
    |||||||
Db 1741 AOSGSVPQKKVYQOEFTDGSFTQPLVYKGLNEHLGLGPLYRAVEENIMVTRRQASR 1800
OY 1801 PYSFYSSLISYEDDQGAEPKRNFKPNETKTYFMKVQHMAPTKDEFDCKAMAYFSDV 1860
    |||||||
Db 1801 PYSFYSSLISYEDDQGAEPKRNFKPNETKTYFMKVQHMAPTKDEFDCKAMAYFSDV 1860
OY 1861 DLEKDVHSLIGPLVCHNTLNPAHGRQVVOEFALFEPIPETKSWTFENNERNCRA 1920
    |||||||
Db 1861 DLEKDVHSLIGPLVCHNTLNPAHGRQVVOEFALFEPIPETKSWTFENNERNCRA 1920
OY 1921 PCNIOMEDPTFKENYRFHAINGYIMDTLPLGLVMAQDQRIWYLLSGNSNENIHSHESGH 1980
    |||||||
Db 1921 PCNIOMEDPTFKENYRFHAINGYIMDTLPLGLVMAQDQRIWYLLSGNSNENIHSHESGH 1980
OY 1981 VETVRKKEEKYKMLVLYPGVEFETVEMLPKAGIMRECELGHEHLHAGSTLEFLVYSKNC 2040
    |||||||
Db 1981 VETVRKKEEKYKMLVLYPGVEFETVEMLPKAGIMRECELGHEHLHAGSTLEFLVYSKNC 2040
OY 2041 QTPLGMA SGHIRDFQITASGQYQWAPKLARLHYS SGINASTKEPFSWIKVDLIAPII 2100
    |||||||
Db 2041 QTPLGMA SGHIRDFQITASGQYQWAPKLARLHYS SGINASTKEPFSWIKVDLIAPII 2100
OY 2101 HGITQGA ROKFSKLTISOFTIMYSLDGKMKQYTRGNSGTGLWVFFGNDSSGKIHNFEN 2160
    |||||||
Db 2101 HGITQGA ROKFSKLTISOFTIMYSLDGKMKQYTRGNSGTGLWVFFGNDSSGKIHNFEN 2160
OY 2161 PPIIARIRLHPHYHISIRSTLMEELMGCDLNSCMP LGMESKASIDAOITTASSTYTNFA 2220
    |||||||
Db 2161 PPIIARIRLHPHYHISIRSTLMEELMGCDLNSCMP LGMESKASIDAOITTASSTYTNFA 2220
OY 2221 TWSPSKARLHLOGRSNANRPQVNNPKEMLAQVFOFKTKKVTGVTQGVKSLTSMYKFEFL 2280
    |||||||
Db 2221 TWSPSKARLHLOGRSNANRPQVNNPKEMLAQVFOFKTKKVTGVTQGVKSLTSMYKFEFL 2280
OY 2281 ISSSQDGHQMTLFPQNGKXKVFQGNQDSFTPVNSIDLPILLITRYLRIHQSSVHQAIALRM 2340
    |||||||
Db 2281 ISSSQDGHQMTLFPQNGKXKVFQGNQDSFTPVNSIDLPILLITRYLRIHQSSVHQAIALRM 2340
OY 2341 EYLGCEAODLY 2351
    |||||||
Db 2341 EYLGCEAODLY 2351

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XX Active Factor VIII:C analogue, delta 1720, 1721, + Pro insertion.
DE Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
XX fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW plasma protease; thrombin; immunogen; antibody; haemophilic therapy;
KW proteolytic cleavage.
XX Homo sapiens.
OS Synthetic.
XX Key Location/Qualifiers
FH Peptide 1..19
FT /note= "signal peptide"
FT Protein 20..2350
FT /note= "mature Factor VIII:C"
FT Region 20..1667
FT /note= "heavy chain fragment"
FT Region 1668..2349
FT /note= "light chain fragment"
FT Domain 759..1667
FT /note= "B domain"
FT Msc-difference 1738..1739
FT /note= "site of 2 residue deletion"
FT Msc-difference 1739
FT /note= "inserted residue"
FT W09703195-A1.
XX 30-JAN-1997.
XX 09-JUL-1996; 96WO-US1444.
XX 11-JUL-1995; 95US-0001025.
XX (CHIR ) CHIRON CORP.
XX Cohen FE, Hung DT, Innis M;
XX WPI: 1997-119050/11.
XX Factor VIII:C analog modified adjacent to a non-activating Arg
XX residue - used in the treatment of haemophilias, by improvement of
XX haemostasis
XX Claim 35; Page -: 90pp; English.
XX AAW11330-W11472 represent active Factor VIII:C analogues of the
XX invention. These sequences were created by mutating the wild type Factor
XX VIII:C coding sequence (see AAT51357) using mutagenic primers. The
XX analogues comprise a native Factor VIII:C polypeptide modified at a site
XX adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
XX dipeptide is created. Factor VIII:C is a large glycoprotein that
XX participates in the blood coagulation cascade that ultimately converts
XX soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
XX deficiency in Factor VIII:C is responsible for haemophilia A, which is an
XX X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
XX activated by plasma proteases, such as thrombin. During activation the
XX mature polypeptide is cleaved to generate heavy and light chain fragments
XX that are further cleaved. Complexes of two or more of the analogues,
XX nucleic acids and vectors encoding them may be used alone or in
XX conjunction with each other, for the prevention or treatment of active
XX Factor VIII:C deficiency in a mammal. The analogues may be used as
XX immunogens to raise antibodies, and in the treatment of haemophilias, by
XX cleavage and display increased plasma half-life. They may be administered
XX at lower dosages and by different modes of administration.
XX Sequence 2350 AA:
SQ

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Query Match 99.8%; Score 12394.5; DB 18; Length 2350;
Best Local Similarity 99.9%; Pred. No. 0;
Matches 2349; Conservative 0; Mismatches 1; Indels 1; Gaps 1;

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Oy 1 MOELSTCFILCLLPFCFSATRRYILGAVELSMQJMSDGLCELPVDAAPPVPKSPFPN 60  
Db 1 MOELSTCFILCLLPFCFSATRRYILGAVELSMQJMSDGLCELPVDAAPPVPKSPFPN 60  
Oy 61 TSVYKKTLLFVEFTDHLFNTAKRPPRMGLGPTIOAEVYDTYVITLKMAASHPPVSLHAV 120  
Db 61 TSVYKKTLLFVEFTDHLFNTAKRPPRMGLGPTIOAEVYDTYVITLKMAASHPPVSLHAV 120  
Oy 121 GVSVMKASEGAEYDDQTSOREKEDDYFPPGSSHTYVMQVILKENGPMASPLCLTYSYLSH 180  
Db 121 GVSVMKASEGAEYDDQTSOREKEDDYFPPGSSHTYVMQVILKENGPMASPLCLTYSYLSH 180  
Oy 181 VDLVYDNLNSGLIGALILCYREGSLAKKERTQTLKFTLLFAVFDCKSMHSTKNSLMORD 240  
Db 181 VDLVYDNLNSGLIGALILCYREGSLAKKERTQTLKFTLLFAVFDCKSMHSTKNSLMORD 240  
Oy 241 AASARAMPKMTYVNGVYVNSLPGLICHRKSVYVHVIGMGTTPVHSIFLEGHTFLVNRH 300  
Db 241 AASARAMPKMTYVNGVYVNSLPGLICHRKSVYVHVIGMGTTPVHSIFLEGHTFLVNRH 300  
Oy 301 ~~MOELSTCFILCLLPFCFSATRRYILGAVELSMQJMSDGLCELPVDAAPPVPKSPFPN~~ 360  
Db 301 ~~MOELSTCFILCLLPFCFSATRRYILGAVELSMQJMSDGLCELPVDAAPPVPKSPFPN~~ 360  
Oy 361 EADYDDDLTDSBMDVYVRFDDNSPSFIOISVAKKHKTYVHTIAAEEEDMDYAPLYLA 420  
Db 361 EADYDDDLTDSBMDVYVRFDDNSPSFIOISVAKKHKTYVHTIAAEEEDMDYAPLYLA 420  
Oy 421 PDDRSYKSOYLNLNGFORIGRKYKRVFMAVDETFKTRREALIOHSGILGLLYGVEGDTL 480  
Db 421 PDDRSYKSOYLNLNGFORIGRKYKRVFMAVDETFKTRREALIOHSGILGLLYGVEGDTL 480  
Oy 481 LIIFKMQASRPYNTYPIHGITDVPRILYSRRLPGVGNHLKDPILILGELFEKKMTVYEDOP 540  
Db 481 LIIFKMQASRPYNTYPIHGITDVPRILYSRRLPGVGNHLKDPILILGELFEKKMTVYEDOP 540  
Oy 541 TKSDPRCLTRYSSSVNNERDLASGLIGLILCYKESYDQGNQIMSKDNVITLESVEDE 600  
Db 541 TKSDPRCLTRYSSSVNNERDLASGLIGLILCYKESYDQGNQIMSKDNVITLESVEDE 600  
Oy 601 NRSWYLTENIORFLPNPAGVOLEDPFOASINMHSINGVYFDSLOLSVCLHEVAAYVYILS 660  
Db 601 NRSWYLTENIORFLPNPAGVOLEDPFOASINMHSINGVYFDSLOLSVCLHEVAAYVYILS 660  
Oy 661 IGAQOTDLSVPFSGYTFPHKKVYEDTLTLPFSGETVPMSENGGLITLICHNSDFRNG 720  
Db 661 IGAQOTDLSVPFSGYTFPHKKVYEDTLTLPFSGETVPMSENGGLITLICHNSDFRNG 720  
Oy 721 MPALLKVVSSCOKNTGDYVEDSYEDISAYILSKNMAIEPRSFONSRRPSTROKQFNATTI 780  
Db 721 MPALLKVVSSCOKNTGDYVEDSYEDISAYILSKNMAIEPRSFONSRRPSTROKQFNATTI 780  
Oy 781 PENDIEKTDPMFAHRTMPKIOYVSSDILLMLROSPTPHGSLSDLOEAKYTFESDDDS 840  
Db 781 PENDIEKTDPMFAHRTMPKIOYVSSDILLMLROSPTPHGSLSDLOEAKYTFESDDDS 840  
Oy 841 PGALDSNNLSBMTFRRPOLHSGDMVFTPESSLOLRINEKLIGTTAATTELKIDFVVSST 900  
Db 841 PGALDSNNLSBMTFRRPOLHSGDMVFTPESSLOLRINEKLIGTTAATTELKIDFVVSST 900  
Oy 901 SNNLSTIPSDNLAAGTDNNTSSLOPPSPMAYHDSOLDTTLFGKSSPPLTESGGPLLSDEE 960  
Db 901 SNNLSTIPSDNLAAGTDNNTSSLOPPSPMAYHDSOLDTTLFGKSSPPLTESGGPLLSDEE 960  
Oy 961 NNDSKLLESGLMNSOESSMKNVSTPSGRLEFGKRAHGAPALLIKNDNALEKVSISLLKTN 1020  
Db 961 NNDSKLLESGLMNSOESSMKNVSTPSGRLEFGKRAHGAPALLIKNDNALEKVSISLLKTN 1020  
Oy 1021 KTSNSATNRKTHIDGPELILIEVSPWONILESSTEEKKYTPLIIDHMLMDKNATAPLRL 1080  
Db 1021 KTSNSATNRKTHIDGPELILIEVSPWONILESSTEEKKYTPLIIDHMLMDKNATAPLRL 1080

Oy 1081 NMSNKTTSKKNMEXVOQKKEGPIPPDAQNPMKSFKKMLFLPESABWIOHTHCKNSLNSG 1140  
Db 1081 NMSNKTTSKKNMEXVOQKKEGPIPPDAQNPMKSFKKMLFLPESABWIOHTHCKNSLNSG 1140  
Oy 1141 QGSPKQOLYSLGPEKSVGQGNFLSEKKNVYVKGGEFTDVLKXMPVPSRNLPLTNLND 1200  
Db 1141 QGSPKQOLYSLGPEKSVGQGNFLSEKKNVYVKGGEFTDVLKXMPVPSRNLPLTNLND 1200  
Oy 1201 LHEBNTHNOEKKIOEEIEKEETLLIOENVYLPQIHVTGKNFKMPLFLSTRONEGSTD 1260  
Db 1201 LHEBNTHNOEKKIOEEIEKEETLLIOENVYLPQIHVTGKNFKMPLFLSTRONEGSTD 1260  
Oy 1261 GAYAPVLODFRSLNDSTNRKTHAHFSKKGEBENLEBIGNOTQOYERKACTTRISPT 1320  
Db 1261 GAYAPVLODFRSLNDSTNRKTHAHFSKKGEBENLEBIGNOTQOYERKACTTRISPT 1320  
Oy 1321 SOONFYTORSKRALKQFRLPLEETELKRIYDDTSTQMSKNMHLPLSTLQIDYNEKE 1380  
Db 1321 SOONFYTORSKRALKQFRLPLEETELKRIYDDTSTQMSKNMHLPLSTLQIDYNEKE 1380  
Oy 1381 KGAITQSPISDCLTRSHSIPQANRSPPLIAKVSPPSIRPIYTLRVLEFDONSHTLPAASY 1440  
Db 1381 KGAITQSPISDCLTRSHSIPQANRSPPLIAKVSPPSIRPIYTLRVLEFDONSHTLPAASY 1440  
Oy 1441 RKDQSVQSSHFLOGAKKNMLSLATILTEPMQDQREVSGTSGTASNTYTKKVENTVLP 1500  
Db 1441 RKDQSVQSSHFLOGAKKNMLSLATILTEPMQDQREVSGTSGTASNTYTKKVENTVLP 1500  
Oy 1501 KPDLPTSCKVELLPKHVILYOKDLFPTETSNGSPGHLDVBCSLQGTBCAIKMEANRP 1560  
Db 1501 KPDLPTSCKVELLPKHVILYOKDLFPTETSNGSPGHLDVBCSLQGTBCAIKMEANRP 1560  
Oy 1561 GKVPFLRVATESSATPESKLLDPLAMNHNHGTQIPEEEMSOEKSPEKTAFFKKDDTILSL 1620  
Db 1561 GKVPFLRVATESSATPESKLLDPLAMNHNHGTQIPEEEMSOEKSPEKTAFFKKDDTILSL 1620  
Oy 1621 NACESNHAALAINBONKPELETYMAKOGTEBTLSONPVLAKHOREIIRTLQSDOEE 1680  
Db 1621 NACESNHAALAINBONKPELETYMAKOGTEBTLSONPVLAKHOREIIRTLQSDOEE 1680  
Oy 1681 IDYDDTISYEMKKEDEFDIYDEDEQSPRSFOKTRHYFAAVERLAMYGMSSSPHYLR -P 1739  
Db 1681 IDYDDTISYEMKKEDEFDIYDEDEQSPRSFOKTRHYFAAVERLAMYGMSSSPHYLR -P 1739  
Oy 1741 AOGSVPOFKKVVPOEFTDGSFTQPLYRGELNHLGLIGPYTIAEVEDNIMYFRRMQASR 1800  
Db 1741 AOGSVPOFKKVVPOEFTDGSFTQPLYRGELNHLGLIGPYTIAEVEDNIMYFRRMQASR 1800  
Oy 1801 PYSTYSSLSYEBDROGAERKRVFVNETKTYFKVQVHMAPTKDEFOCKMAATFSVY 1860  
Db 1801 PYSTYSSLSYEBDROGAERKRVFVNETKTYFKVQVHMAPTKDEFOCKMAATFSVY 1860  
Oy 1861 DLEKDVHSGILGPLVCHTNTLNAHGRQYVQEFALFPTJFDETAKSVFTENNERNCRA 1920  
Db 1861 DLEKDVHSGILGPLVCHTNTLNAHGRQYVQEFALFPTJFDETAKSVFTENNERNCRA 1920  
Oy 1921 PCNTOMEDPPEKENTRFAINGYIMOTLPLJMAOORIRAWYLLSMGSNNHISHIFPSH 1980  
Db 1921 PCNTOMEDPPEKENTRFAINGYIMOTLPLJMAOORIRAWYLLSMGSNNHISHIFPSH 1980  
Oy 1980 VFTVVRKKEEYKNAALYNLYPGVFEVEMLPKAGIMVEBCLJGEHILHGMSTLELVYSNKC 2039  
Db 1980 VFTVVRKKEEYKNAALYNLYPGVFEVEMLPKAGIMVEBCLJGEHILHGMSTLELVYSNKC 2039  
Oy 2041 QTPLGMASSHIRDPQITASGOYGOMAKLARLYSGSISIANMSTKEPFSWIKVLDLPMII 2100  
Db 2041 QTPLGMASSHIRDPQITASGOYGOMAKLARLYSGSISIANMSTKEPFSWIKVLDLPMII 2100  
Oy 2101 HGITQGAQKSSSLYIQOTILNLSLQKQWQYRONSNGTLPMPFGVQSSGKIKHIN 2160  
Db 2101 HGITQGAQKSSSLYIQOTILNLSLQKQWQYRONSNGTLPMPFGVQSSGKIKHIN 2160  
Oy 2161 PPIIARYIRLHPHTYIRSITLMBELMCDLNSCMPJLGMESKASISDAQITASSYFTNMPA 2220  
Db 2161 PPIIARYIRLHPHTYIRSITLMBELMCDLNSCMPJLGMESKASISDAQITASSYFTNMPA 2220

|||||  
DB 2160 PPIARIYRLHPTHTYSISITLMEIMGCDLNSCSMPLEGESKAISDAOITFASSTFMMFA 2219  
QY 2221 TWSPSKARLHLOGRSNAMPPOVNNPKEMLOVDOKTKMTKVTGVTGQVKSLLTSMTVKEFL 2280  
DB 2220 TWSPSKARLHLOGRSNAMPPOVNNPKEMLOVDOKTKMTKVTGVTGQVKSLLTSMTVKEFL 2279  
QY 2281 ISSSQDGHQWTLFFQNGKVKVFOGNOSEFPVYVNSLDPLRLTRYLRHPQSVHQAIALRM 2340  
DB 2280 ISSSQDGHQWTLFFQNGKVKVFOGNOSEFPVYVNSLDPLRLTRYLRHPQSVHQAIALRM 2339  
QY 2341 EYLGCSEAODLY 2351  
DB 2340 EYLGCSEAODLY 2350

RESULT 100

AAW11380  
ID AAW11380 standard; Protein; 2350 AA.

XX AAW11380;

DT 18-NOV-1997 (first entry)

XX Active Factor VIII:C analogue, delta 335, + P333X.

XX Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;

KM fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;

KM plasma protease; thrombin; immunogen; antibody; haemophilia; therapy;

XX proteolytic cleavage.

XX Homo sapiens.

OS Synthetic.

XX Location/Qualifiers

FT Peptide 1..19 /note= "signal peptide"

FT Protein 20..2350 /note= "mature Factor VIII:C"

FT Region 20..1666 /note= "heavy chain fragment"

FT Modified-site 352 /label= "Phe, Glu"

FT Misc-difference 353..354 /note= "site of 1 residue deletion"

FT Region 1667..2349 /note= "light chain fragment"

FT Domain 759..1666 /note= "B domain"

XX MO9703195-A1.

XX 30-JAN-1997.

XX 09-JUL-1996; 96MO-US11444.

XX 11-JUL-1995; 95US-0001025.

XX (CHIR ) CHIRON CORP.

XX Cohen FE, Hung DT, Innis M;

XX WPI; 1997-119050/11.

XX Factor VIII:C analog modified adjacent to a non-activating Arg

CC residue - used in the treatment of haemophiliacs, by improvement of

CC haemostasis

XX Claim 18; Page -: 90pp; English.

XX AAW11330-W11472 represent active Factor VIII:C analogues of the

CC invention. These sequences were created by mutating the wild type Factor

CC analogues comprise a native Factor VIII:C polypeptide modified at a site  
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg  
CC dipeptide is created. Factor VIII:C is a large glycoprotein that  
CC participates in the blood coagulation cascade that ultimately converts  
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A  
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an  
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is  
CC activated by plasma proteases, such as thrombin. During activation the  
CC mature polypeptide is cleaved to generate heavy and light chain fragments  
CC that are further cleaved. Complexes of two or more of the analogues,  
CC nucleic acids and vectors encoding them may be used alone or in  
CC conjunction with each other, for the prevention or treatment of active  
CC Factor VIII:C deficiency in a mammal. The analogues may be used as  
CC immunogens to raise antibodies, and in the treatment of haemophiliacs, by  
CC improvement of haemostasis. The analogues are resistant to proteolytic  
CC cleavage and display increased plasma half-life. They may be administered  
CC at lower dosages and by different modes of administration.

XX Sequence 2350 AA;

Query Match 99.8%; Score 12394.5; DB 18; Length 2350;

Best Local Similarity 99.9%; Pred. No. 0; Matches 2349; Conservative 0; Mismatches 1; Indels 1; Gaps 1;

QY 1 MQIELSTCFELCLLRFCSATRRYYLGAAYELISMDYMOGDLGELPVDAAPPVRYKSPFN 60  
DB 1 MQIELSTCFELCLLRFCSATRRYYLGAAYELISMDYMOGDLGELPVDAAPPVRYKSPFN 60  
QY 61 TSVVYKTLFEVFTDHLFNIAKPRPPMGLGPTIOAEVYDTVVITLKNASHPVSLAAV 120  
DB 61 TSVVYKTLFEVFTDHLFNIAKPRPPMGLGPTIOAEVYDTVVITLKNASHPVSLAAV 120  
QY 121 GVSYWKASGAEYDQPSQREKEDKVFQGGSGHTVWVOYLKENGPMASDPICLTYSYLSH 180  
DB 121 GVSYWKASGAEYDQPSQREKEDKVFQGGSGHTVWVOYLKENGPMASDPICLTYSYLSH 180  
QY 181 VDLVKDNLGSLGALLVYCREGSLAKEKTOYTLKFIILFAVDEGKSMHSETKNSLMQDRD 240  
DB 181 VDLVKDNLGSLGALLVYCREGSLAKEKTOYTLKFIILFAVDEGKSMHSETKNSLMQDRD 240  
QY 241 AASARAMPKMTVNGVYVRSRPLGICGRKSVYWHYGTTPEVNSIFLEGHTFLVRNH 300  
DB 241 AASARAMPKMTVNGVYVRSRPLGICGRKSVYWHYGTTPEVNSIFLEGHTFLVRNH 300  
QY 241 AASARAMPKMTVNGVYVRSRPLGICGRKSVYWHYGTTPEVNSIFLEGHTFLVRNH 300  
DB 241 AASARAMPKMTVNGVYVRSRPLGICGRKSVYWHYGTTPEVNSIFLEGHTFLVRNH 300  
QY 301 ROASLEISPTFLTAOTLLMDLGOFLFCHISSHQDGEAYVYKDSCEPPOLRKKNNE 360  
DB 301 ROASLEISPTFLTAOTLLMDLGOFLFCHISSHQDGEAYVYKDSCEPPOLRKKNNE 360  
QY 361 EARDYDDDLTDEEMVYVRFDDNSPFIQIRSAVAKKHPRKTWVHYIAAEEDMDYAPLYLA 420  
DB 361 EARDYDDDLTDEEMVYVRFDDNSPFIQIRSAVAKKHPRKTWVHYIAAEEDMDYAPLYLA 420  
QY 421 PDDRSYKSOYLLNNGPQIRGRYKRVYRMAYTDETFKTRAIQIHESGILGPLLVEGVDTL 480  
DB 421 PDDRSYKSOYLLNNGPQIRGRYKRVYRMAYTDETFKTRAIQIHESGILGPLLVEGVDTL 480  
QY 481 LIIFKNQASRPYNIIPHGLTDVRLPYRRLPKGVKILKDFPLIPGLPEIFKRYKWTVEDEGP 540  
DB 481 LIIFKNQASRPYNIIPHGLTDVRLPYRRLPKGVKILKDFPLIPGLPEIFKRYKWTVEDEGP 540  
QY 541 TKSDPRCLTRYISYVNNKRDLAGSLIGPLLTCKRSVQORNOIMSDKRVILFSEVDE 600  
DB 541 TKSDPRCLTRYISYVNNKRDLAGSLIGPLLTCKRSVQORNOIMSDKRVILFSEVDE 600  
QY 601 NRSWYLTENIORFLNPNAGVOLLEDPERQASINHSINGYVPSLOLSVCLAEVAYWYIIS 660  
DB 601 NRSWYLTENIORFLNPNAGVOLLEDPERQASINHSINGYVPSLOLSVCLAEVAYWYIIS 660  
QY 661 IGAOTDFLSVFSFGYTFKHKMYEDTILTFPSGSEVFMSEMPGLMILGCHNSDFNRNG 720  
DB 661 IGAOTDFLSVFSFGYTFKHKMYEDTILTFPSGSEVFMSEMPGLMILGCHNSDFNRNG 720  
QY 721 MTALKVSSCDKNWGTGYEDSYEDISAYLLSKNNAIEPRFSQNSRHSRSTROKOFNATYTI 780  
DB 721 MTALKVSSCDKNWGTGYEDSYEDISAYLLSKNNAIEPRFSQNSRHSRSTROKOFNATYTI 780



Db	720	MTALLKVS	CDKNTD	YEDSYED	ISAYLL	SKNNAI	IEPR	SFSQ	SRHP	STROQ	AFNAT	779										
Qy	781	PENDIEK	TDPM	FAHRT	MPK	IONVSS	DLML	ROS	SP	PHG	LS	DLQ	EAK	YET	FSD	840						
Db	780	PENDIEK	TDPM	FAHRT	MPK	IONVSS	DLML	ROS	SP	PHG	LS	DLQ	EAK	YET	FSD	839						
Qy	841	PGAI	DNNS	LEBMT	HFR	POL	HSG	DV	FT	PES	GL	RL	NEK	IG	TTA	TEAK	LD	FV	YS	900		
Db	840	PGAI	DNNS	LEBMT	HFR	POL	HSG	DV	FT	PES	GL	RL	NEK	IG	TTA	TEAK	LD	FV	YS	899		
Qy	901	SNN	LSTI	PS	DN	LA	AG	DN	TSS	LC	PS	MV	HN	D	S	LD	TT	LG	K	S	960	
Db	900	SNN	LSTI	PS	DN	LA	AG	DN	TSS	LC	PS	MV	HN	D	S	LD	TT	LG	K	S	959	
Qy	961	NND	SK	LES	G	L	M	S	O	E	S	S	M	G	K	N	V	S	T	E	S	1020
Db	960	NND	SK	LES	G	L	M	S	O	E	S	S	M	G	K	N	V	S	T	E	S	1019
Qy	1021	KTS	NN	S	A	T	N	R	K	T	H	I	D	G	S	L	I	E	N	S	P	1080
Db	1020	KTS	NN	S	A	T	N	R	K	T	H	I	D	G	S	L	I	E	N	S	P	1079
Qy	1081	NH	S	K	T	T	S	K	N	M	E	V	O	O	K	E	G	P	I	P	D	1140
Db	1080	NH	S	K	T	T	S	K	N	M	E	V	O	O	K	E	G	P	I	P	D	1139
Qy	1141	OG	P	S	P	K	O	L	V	S	I	G	P	E	K	S	V	E	G	O	N	1200
Db	1140	OG	P	S	P	K	O	L	V	S	I	G	P	E	K	S	V	E	G	O	N	1199
Qy	1201	LH	E	N	T	H	O	E	K	I	O	E	B	E	I	E	K	E	T	I	O	1260
Db	1200	LH	E	N	T	H	O	E	K	I	O	E	B	E	I	E	K	E	T	I	O	1259
Qy	1261	G	A	V	A	P	L	O	D	F	R	S	L	N	D	S	T	N	R	T		1320
Db	1260	G	A	V	A	P	L	O	D	F	R	S	L	N	D	S	T	N	R	T		1319
Qy	1321	S	O	O	N	F	T	O	R	S	K	R	A	L	K	O	R	L	E	T	E	1380
Db	1320	S	O	O	N	F	T	O	R	S	K	R	A	L	K	O	R	L	E	T	E	1379
Qy	1381	K	G	A	I	T	O	S	P	L	S	D	C	L	R	S	H	I	P	O	A	1440
Db	1380	K	G	A	I	T	O	S	P	L	S	D	C	L	R	S	H	I	P	O	A	1439
Qy	1441	R	K	K	D	S	G	V	O	E	S	H	I	O	G	A	K	N	N	L	S	1500
Db	1440	R	K	K	D	S	G	V	O	E	S	H	I	O	G	A	K	N	N	L	S	1499
Qy	1501	K	P	D	L	P	K	T	S	G	K	V	E	L	L	P	K	V	H	I	O	1560
Db	1500	K	P	D	L	P	K	T	S	G	K	V	E	L	L	P	K	V	H	I	O	1559
Qy	1561	G	K	V	P	L	R	A	T	E	S	S	A	K	T	S	K	L	D	P	L	1620
Db	1560	G	K	V	P	L	R	A	T	E	S	S	A	K	T	S	K	L	D	P	L	1619
Qy	1621	N	A	C	E	S	N	H	A	I	A	I	N	G	O	K	P	E	I	E	V	1680
Db	1620	N	A	C	E	S	N	H	A	I	A	I	N	G	O	K	P	E	I	E	V	1679
Qy	1681	I	D	Y	D	T	I	S	V	E	M	K	K	E	D	P	I	Y	D	E	N	1740
Db	1680	I	D	Y	D	T	I	S	V	E	M	K	K	E	D	P	I	Y	D	E	N	1739
Qy	1741	A	O	S	G	S	V	P	O	F	K	V	Y	O	E	F	T	D	S	F	T	1800
Db	1740	A	O	S	G	S	V	P	O	F	K	V	Y	O	E	F	T	D	S	F	T	1799
Qy	1801	P	S	F	S	S	L	I	S	E	E	D	O	R	G	A	P	R	K	N	F	1860
Db																						

Db	1800	P	S	F	S	S	L	I	S	E	E	D	O	R	G	A	P	R	K	N	F	1859
Qy	1861	D	L	E	K	D	V	H	S	G	L	I	G	P	L	V	C	H	N	T	L	1920
Db	1860	D	L	E	K	D	V	H	S	G	L	I	G	P	L	V	C	H	N	T	L	1919
Qy	1921	P	C	N	I	O	M	E	D	P	F	F	K	E	N	F	H	A	I	N	G	1980
Db	1920	P	C	N	I	O	M	E	D	P	F	F	K	E	N	F	H	A	I	N	G	1979
Qy	1981	V	F	T	Y	K	K	E	E	R	K	M	A	L	N	L	I	P	G	V	E	2040
Db	1980	V	F	T	Y	K	K	E	E	R	K	M	A	L	N	L	I	P	G	V	E	2039
Qy	2041	O	T	P	L	G	A	S	G	H	I	R	D	F	O	I	T	A	S	G	O	2100
Db	2040	O	T	P	L	G	A	S	G	H	I	R	D	F	O	I	T	A	S	G	O	2099
Qy	2101	H	G	I	T	O	G	A	R	O	K	F	S	S	L	I	S	O	F	I	M	2160
Db	2100	H	G	I	T	O	G	A	R	O	K	F	S	S	L	I	S	O	F	I	M	2159
Qy	2161	P	P	I	A	R	I	R	L	P	T	H	S	I	R	S	T	L	R	M	E	2220
Db	2160	P	P	I	A	R	I	R	L	P	T	H	S	I	R	S	T	L	R	M	E	2219
Qy	2221	T	W	S	P	S	K	A	R	L	H	O	G	R	S	N	A	M	R	P	O	2280
Db	2220	T	W	S	P	S	K	A	R	L	H	O	G	R	S	N	A	M	R	P	O	2279
Qy	2281	I	S	S	O	D	H	O	M	T	F	F	O	N	G	K	V	F	O	G	2340	
Db	2280	I	S	S	O	D	H	O	M	T	F	F	O	N	G	K	V	F	O	G	2339	
Qy	2341	E	V	L	C	E	A	O	D	L	Y										2351	
Db	2340	E	V	L	C	E	A	O	D	L	Y										2350	

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Job time : 166 secs

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Job time : 166 secs

